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# GUY'S HOSPITAL REPORTS.

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- Hygienic Laboratory and Yellow Fever Institute Bulletins (care of Smithsonian Institution, Washington, D.C., U.S.A.), per Messrs. W. Wesley & Son, 28, Essex Street, Strand, W.C.

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M. Felix Alcan, 108, Boulevard St. Germain, Paris)

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S.W.)

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Chelsea Bridge Road, S.W. (care of The Secretary)

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Bellecour, Lyons)



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(Reprinted from the *Quarterly Journal of Medicine*, July, 1908,  
Vol. I., No. 4.)

## ON PADS ON THE FINGER JOINTS.

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By

W. HALE WHITE, M.D.

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From time to time we see people who have pads upon the dorsal aspect of the joints between the first and second phalanges of the fingers. A. E. Garrod<sup>1</sup> called attention to them in 1893 and 1904. From my own observation I can corroborate all he says about them. They are usually present on some of the joints of both hands, and they may be on all eight joints; but all the joints need not be affected. They vary in size from a split pea to a hazel-nut. Their appearance is well shown in Fig. 1. I myself have never seen them on any other joint, but it is said that very occasionally they may be seen on the terminal phalangeal joints. It need hardly be said that care must be taken when they occur here to distinguish them from Heberden's nodes. They are quite different from these, for they occur at the back of the joint, they are soft, and they can be moved about on the subjacent bone, and do not at all feel as though they were connected with this. They are usually painless, but at times some patients complain of pain and tenderness in them. When once they have formed they are permanent, and they take a few weeks or months to attain their permanent size. Of Garrod's twelve cases, seven were in males, five were in females. Six of the patients had Dupuytren's contraction of the palmar fascia, but the pads nearly always

<sup>1</sup> A. E. Garrod, *St. Bartholomew's Hospital Reports*, 1893, vol. xxix., p. 157; *British Medical Journal*, July 2, 1904, p. 8.

develop at an earlier period of life than the contraction of the palmar fascia. Apart from this association, it is not known that these pads have relationship to any disease. My only justification for publishing a single case is that I am able to supply the first histological account of these pads.

The patient, an officer in the army, was aged 43 when I saw him. He had well-developed Dupuytren's contraction of the palmar fascia of both hands. He first noticed the commencement of this contraction in the left hand two years ago, and it has progressed uniformly since. Eighteen months ago he first observed, on both hands, small lumps on the backs of the joints between the first and second phalanges. A year ago contraction of the palmar fascia of the right hand began: it is now considerable, and of greater extent than that of the left. Fig. 2 shows its condition in the right hand when I saw him. The pads are situated only on the joints between the first and second phalanges. On the right hand there is one the size of a Barcelona nut on the index-finger; the next finger has not got one, but on the ring-finger there is one the size of a pea, and on the little finger there is one which is much swollen. On the left hand there is one on the index-finger the size of a small pea, the next finger has one the size of a large pea, the ring-finger none, and the little finger one the size of a small pea. The appearance of these lumps on the left hand is well shown in Fig. 1. The skin over all is movable, and each pad feels to be unconnected with the subjacent bone. That this is so is shown by the X-ray photographs, for which I am indebted to Dr. Hugh Walsham (Figs. 3 and 4). The pads are slightly movable upon the subjacent bone. Each is somewhat soft, indeed sufficiently soft to suggest the possibility that it contains some fluid; but a year ago one had been incised by a doctor, and no fluid was evacuated. The scar of the incision can be seen; it healed perfectly. The patient says that after the incision the lump was a little smaller, but now it is bigger than ever. None of the lumps are painful or tender; there is no evidence that the patient has ever had gout, and, except for the condition of the hands, he is perfectly healthy.

Mr. Charters Symonds excised the palmar fascia of one of the hands, and the patient kindly allowed him to excise one of the pads. A drawing of the microscopical appearances of this, by Dr. T. G. Stevens, is shown in Fig. 5.

It is seen that there is a great hypertrophy of the corneous layer of the epithelium. Considering that these pads, being prominent on the knuckles, must have been subjected to friction, this is what we should have expected. The stratum granulosum is very distinct, and there appears to be nothing abnormal in the rete mucosum. There is no alteration in the papillæ, which shows that the pads are not of the nature of corns. The corium appears natural, but under it is a quantity of richly nucleated, not very vascular, fibrous tissue, constituting the tumour. The nuclei and the interlacing bundles of the fibrous tissue are very well seen in the figure. No sweat glands were noticed in the section, and there was no evidence that the tumour was inflammatory. Subcutaneous fibromata, which are very common in various parts of the body, often show inflammatory changes, but these pads do not appear to be a variety of these fibromata. Indeed, they are a pure new growth of fibrous tissue, with some thickening of the stratum corneum; this, however, is probably secondary, and merely due to friction.

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#### EXPLANATION OF FIGURES.

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Fig. 1.—Shows the pads on the proximal interphalangeal joints of left hand.

Fig. 2.—Shows the Dupuytren's contraction of the right palmar fascia.

Figs. 3 and 4 are X-ray photographs showing that the pads are unconnected with the subjacent joints.

Fig. 5.—Shows the histological appearance of one of the pads.



*On Pads on the Finger Joints.*



Fig. 1.

U of M



Mr. U



Fig. 2.

WFOU

*On Pads on the Finger Joints.*

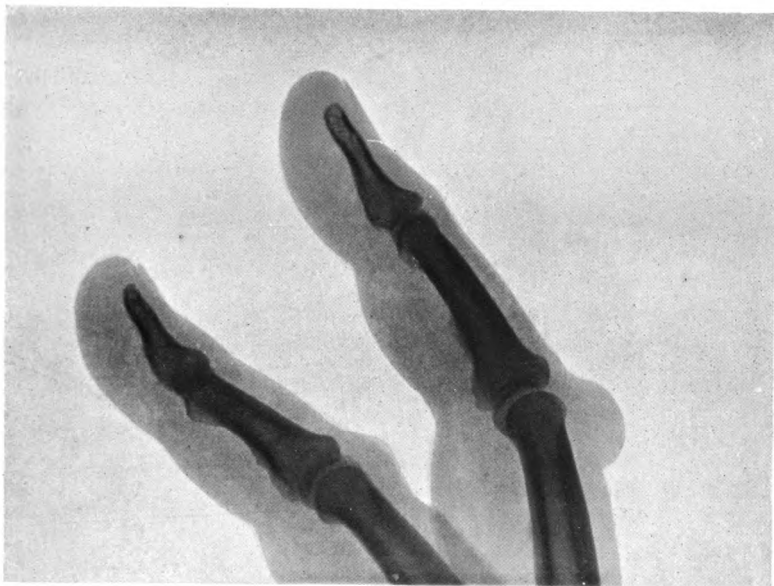


Fig. 3.

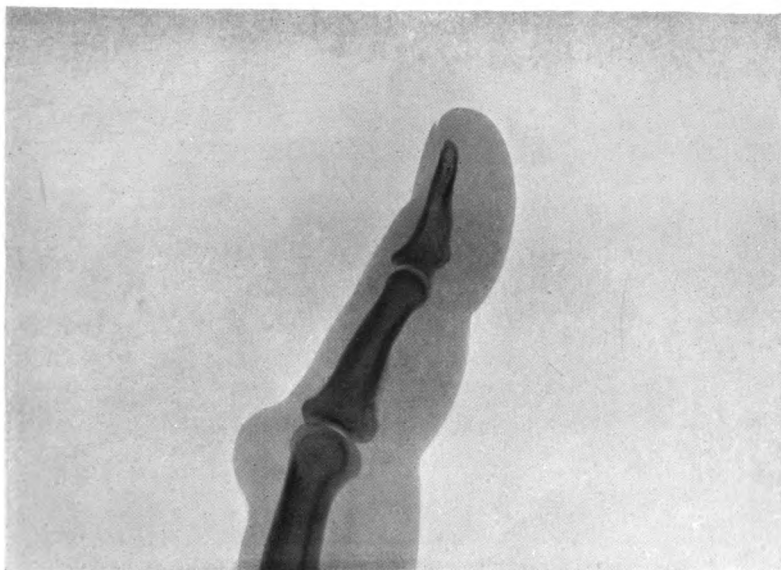


Fig. 4.

U of M

Mr. U

*On Pads on the Finger Joints.*

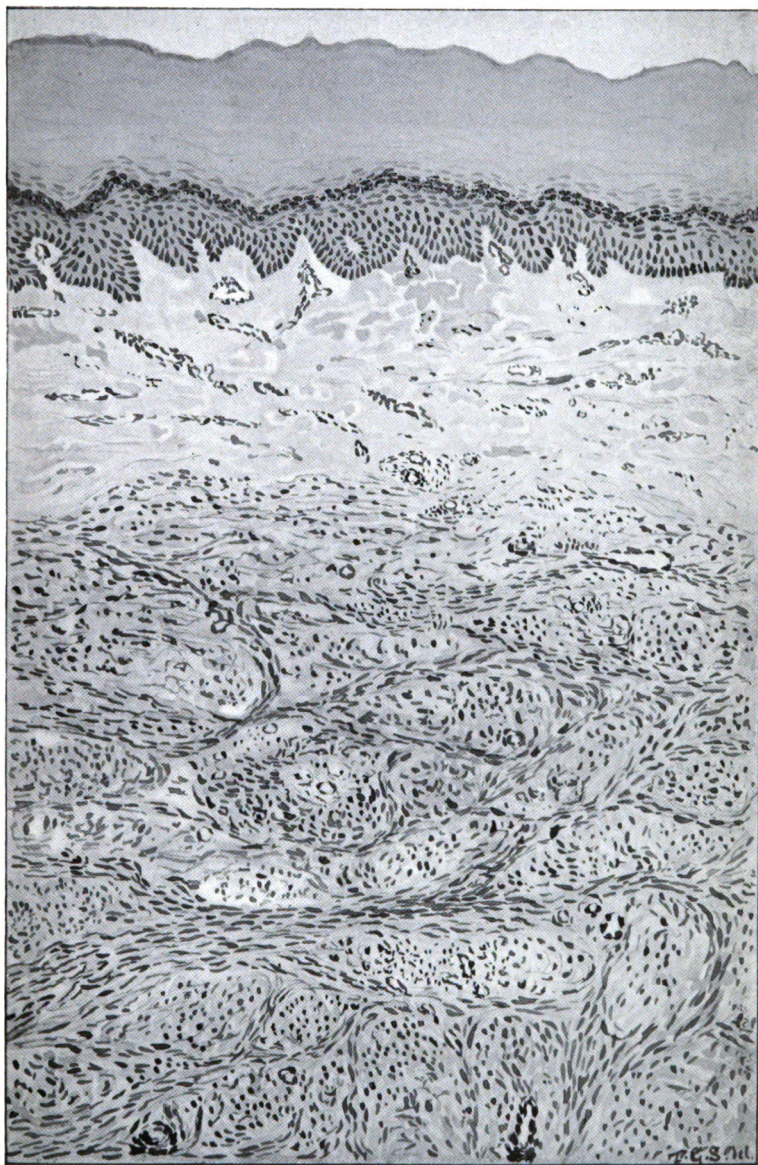


Fig. 5.

U. of M.

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# PERSISTENT HEREDITARY CEDEMA OF THE LEGS WITH ACUTE EXACERBATIONS. MILROY'S DISEASE.

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By

W. B. HOPE, M.R.C.S., L.R.C.P.

AND

HERBERT FRENCH, M.A., M.D., F.R.C.P.

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THE case which has led us to write this paper is as follows:—

Alice W., aged 18, was sent up to Guy's Hospital in 1906, having been under observation at Caversham for seven years previously. Her family history is remarkable; it is given a place to itself later in the paper. The patient was quite normal-looking when born, but in 1888, when three months old, she was noticed to have swollen feet, and apparently there was no cause for the swelling. It was recognised by the parents as being the beginning of the family complaint. The child grew up in the usual way, and there is no clear history of how the "œdema" spread; but it is definitely stated that the swelling, though varying in amount from time to time, never went quite away, and it slowly became more persistent and extensive. By 1899, when she was eleven years old, both legs, from knees to toes,



were so swollen that she had to wear bandages. The latter kept the swelling down to some extent; without bandages the legs became enormous. Her only other trouble was a chronic inflammation of the eyelids, dating from birth. The general health was not interfered with, and when the legs were bandaged she could get about quite well. At no time was there œdema elsewhere than in the legs. There was no breathlessness, no tendency to chilblains, no gastro-intestinal disorder sufficient to attract attention, no suggestion of Raynaud's phenomena, no urticaria, indeed nothing but apparently causeless firm swelling of the legs of the nature of semi-solid œdema. This affection being common in the family, little attention was paid to it; and when, in August, 1900, she first saw Mr. Hope, it was not on account of her legs, but of her eyes—an exacerbation of the blepharitis which she had had all her life. Ophthalmoscopic examination showed healthy optic discs and retinae; both ocular and palpebral conjunctivæ were injected from an acute conjunctivitis which had recently developed upon a chronic blepharitis. Vision was  $\frac{5}{16}$  in each eye, and there was slight photophobia. The acute conjunctivitis was soon relieved, though the chronic blepharitis persisted as before. It seemed that the conjunctival condition was, in a sense, accidental, and not directly connected with the swelling of the legs. The latter had the appearance of moderate elephantiasis, similar to, but less in degree than, their condition in 1906. They remained in much the same state from 1899 to 1904, and then occurred the first of a series of "acute attacks" of pain and additional swelling.

We propose to give a somewhat detailed account of these "acute attacks," because they have not occurred, or, at least, they have not been prominent features, in the similar cases of hereditary trophœdema recorded by Milroy, Meigs, Rolleston, and others.

*The first "acute attack"* occurred on January 19th, 1904. The patient at first noticed an acute pain in her pudenda, but did not regard it as serious. The next day she walked to a neighbouring town, and this made the pain in the pudenda so much worse that she had much difficulty in walking back again.

When she got home she went to bed. Her temperature was only 97.4° F., and her pulse rate 74 per minute, but she was shivering in spite of hot-water bottles in the bed. The pudenda were generally swollen and painful, especially the left labium minus, and there was a red patch over the metatarso-phalangeal joint of the right great toe. The swelling of the legs was not materially increased at the time, and the local condition gradually improved until, by January 26th, she had practically recovered from the acute attack, the pudenda had become normal again, pain was gone, and the legs were as before—chronically swollen from the knees downwards.

This was the only occasion on which the pudenda have been affected at all, and also the only occasion on which there was no rise of temperature during one of these acute attacks.

The second "acute attack" began on June 10th, 1904. At 6 a.m. the patient had a severe fit of shivering, which lasted an hour and a half. She then vomited four times at short intervals, after which she became very hot, and experienced severe continuous pain down her right thigh and leg, from Poupart's ligament to the ankle. Her temperature was 104° F., her pulse rate 126, and her respiration 52 per minute. The right thigh, leg, and foot, beginning sharply at Poupart's ligament, were red, enormously swollen, very hot to the touch, painful, and so tender that any pressure that could be borne failed to cause any pitting. The left thigh and leg felt hot also, but they were neither red nor painful, and the swelling on the left side was only the same as had been present for years. The measurements taken at the time showed:—

*Maximum circumference measurements.*

	Right side.	Left side.
Instep	18 inches.	12 inches.
Calf	16 $\frac{1}{2}$ "	17 $\frac{1}{4}$ "
Knee	21 $\frac{1}{2}$ "	21 $\frac{1}{8}$ "
Thigh	23 $\frac{1}{2}$ "	24 $\frac{1}{4}$ "

We have no record of measurements previously to this, but clinically the left leg had always been considerably more bulky than the right hitherto.

There were no abnormal physical signs in the lungs nor in the abdominal organs. The only abnormal physical sign noted in the heart was a faint blowing systolic murmur, which was heard both at the impulse and at the base; it was thought not to indicate any valvular disease.

Next day, June 11th, 1904, the temperature had fallen to 100° F., the pulse rate to 106, the respiration rate to 40. The right lower limb was still hotter than the left, the redness above the knee had disappeared, and that below the knee was fading markedly. Pain was also much less.

On June 12th, 1904, the systolic bruits were scarcely to be detected. The temperature was 99° F., the pulse rate 100, and the respiration rate 20 per minute. The right lower limb was desquamating, and the pain in it was almost gone.

By June 16th, 1904, the attack was quite over, the temperature was 98° F., the pulse rate 60, and the respiration rate 20 per minute.

Measurements showed:—

*Maximum circumference measurements.*

	Right leg.	Left leg.
Instep	11½ inches.	10½ inches.
Calf	14½ "	14½ "
Knee	17 "	16½ "
Thigh	21 "	21½ "

Both legs had diminished in size, as was always the case, to some extent, when the patient lay in bed for a week.

The third "acute attack" occurred on August 22nd, 1904, and was very similar to the second. It may be noted that, up to this time, there had been no breach of surface in either leg, no boil nor sore place that could be detected, and no enlarged lymphatic glands in the groins or elsewhere. The urine had a specific gravity of 1010; it was pale and clear, with a neutral reaction, and it contained neither albumen nor sugar.

The first breach of surface that was noticed was some time after the patient had been up and about after recovery from the third "acute attack;" on November 1st, 1904, there were



*Persistent Hereditary Œdema of the Legs with  
Acute Exacerbations. Milroy's Disease.*

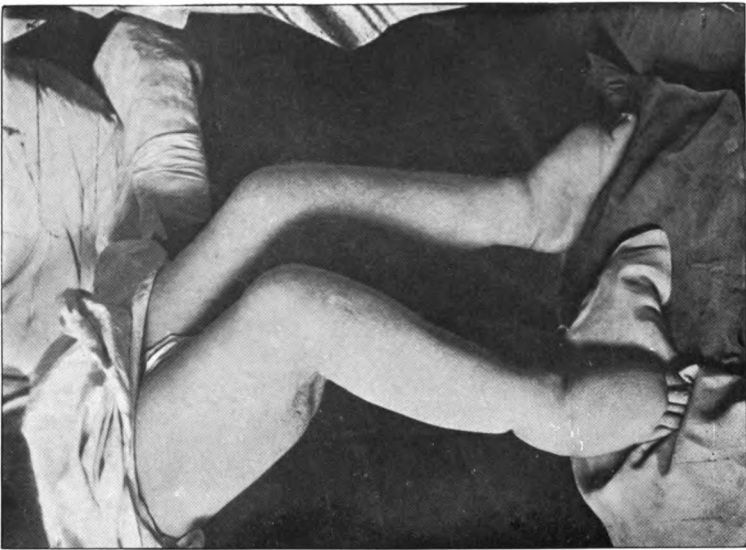


FIG. 2.

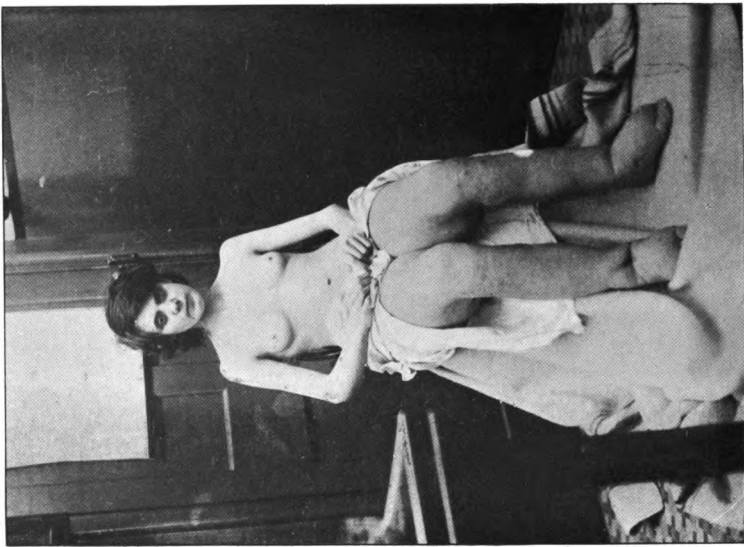


FIG. 1.

numerous small superficial ulcers in the skin about both knees. These ulcers were mostly no more than an eighth of an inch in diameter, the largest measuring half an inch across; each had a sloughy base, an indefinite edge, and a thin serous discharge, which was small in amount. Each excoriation was surrounded by an area of redness due to inflammation. There was nothing suggestive of syphilis in the appearance of the very shallow sore places; they seemed to be pyodermic from accidental infection of the poorly-nourished skin.

*The fourth "acute attack."* On November 4th, 1904, about 3 p.m., the patient complained of shivering, and of severe pain down her left side. Half an hour later both lower limbs became hot and began to swell. A typical attack followed, like the previous ones in every respect, except that both legs were affected equally instead of one more than the other.

*The fifth, sixth, seventh, eighth, ninth, and tenth "acute attacks."* These occurred at intervals of a month or two during the year 1905. Each was confined to the right leg, was of short duration, and very similar to those already described. It is worthy of note that the patient was now eighteen years of age, and had only menstruated once.

A short but acute attack of mental derangement occurred in February, 1906. On February 19th of that year she became very excited and talkative, without apparent cause, and next day she was garrulous, with a happy, but unintelligent, facial expression, much exaltation, and delusions. The following day, February 20th, she was passing her motions and urine under her, and she had delusions about money. On February 21st she was very noisy, and persistently dirty in her habits. She continued in this abnormal mental condition throughout March, April, and May, but in June she gradually improved, and entirely regained her reason.

She was in Guy's Hospital from November 1st to December 1st, 1906. The condition of her legs at that time is shown in the accompanying photographs (Figs. 1 and 2).

There was brawny, elephantiasis-like swelling of the whole of both lower extremities, from Poupart's ligament and the gluteal

fold above to the toes below. The pudenda were not affected, nor did the swelling extend on to the trunk. If any parts of the lower limbs were less affected than the rest, they were the plantar surfaces of the feet and toes themselves. The swelling appeared to be subcutaneous, the skin itself being dry, but only moderately thickened, and not discoloured. The swelling obliterated the normal outlines of the parts, bony prominences, such as the malleoli, the patellæ, and the great trochanters, not being made out. The swelling was comparatively uniform in the straight parts of each limb, with deep transverse sulci across the roots of the toes, in front of and behind the ankles, and behind the knees. On lightly handling the parts they felt almost hard, but on firmly pressing with the finger, for a longer time than is necessary in the case of ordinary œdema, deep pitting was obtainable, so that, even if there was a real increase in the subcutaneous connective tissues, there was considerable œdema as well, of the kind that is sometimes called semi-solid.

The legs were skiagraphed, and the X-rays showed no abnormality in the bones. It was impossible to examine the muscles digitally; they were certainly deficient in power, for the patient could stand with difficulty and could scarcely walk at all. It seemed likely, however, that this apparent weakness of the muscles might well be due to the mechanical difficulties in the way of their free action rather than to any real disease in the muscle fibres themselves. The electrical reactions were tested, but the resistance in the dry coarse skin was so great that no contraction was obtainable with any current, faradic or galvanic, that the patient could bear over the quadriceps extensor femoris, or the ham-string muscles of the legs. The tibialis anticus muscles responded to a bearable faradic current, and so did the long extensors of the toes and the muscles at the back of the calf, though the resultant movements of the toes or ankles were but slight. These muscles also gave a slight galvanic reaction, in which the kathodal closure contraction was more easily obtained than the anodal closure contraction. So far as could be judged, therefore, the electrical reactions were normal, though the difficulties in the way of obtaining them were great. The

muscles of the upper extremities all gave a normal reaction with readiness.

As regards sensation, there was no abnormality. Cutaneous sensibility was present everywhere, and localization was correct. Heat and cold were properly distinguished, pain was felt distinct from touch, muscle sense was correct, and pressure sense was normal when allowance for the thickness of the superficial tissues was made. There was no cutaneous hyperæsthesia, and there was no pain at all. The feet themselves were not markedly colder than those of other patients in the wards at the same time.

The respiratory system was perfectly natural.

The alimentary system was apparently sound. The tongue was clean and moist, the teeth good, the appetite good; there was no tendency to nausea or vomiting, and the bowels were opened regularly. Neither liver nor spleen could be felt; indeed, no abnormality could be made out, and the abdominal wall was supple and natural right down to Poupart's ligament, where the swelling of the legs suddenly began.

The genital system was abnormal only in respect to menstruation, which had occurred but once, though the patient was eighteen.

The urine was also natural; its specific gravity was 1014, its colour pale yellow, its reaction acid; it was clear, of normal amount, and it contained no albumen, blood, pus, or sugar; microscopical examination showed no abnormal constituents. No excess of indican was present.

The temperature varied from 97° F. to 98·8° F., being for the most part slightly sub-normal. The pulse rate varied from 66 to 88, and the respiration rate from 20 to 24 per minute.

The heart appeared to be of normal size, and the sounds were clear and entirely free from bruit. The peripheral arteries that could be felt were natural; the maximum systolic blood pressure in the brachial artery, taken on many different occasions by Martin's modification of the Riva-Rocci apparatus, was never higher than 132 mm., and never lower than 120 mm. of mercury. There were no varicose or other distended veins to be seen anywhere, nor were there any telangiectases. The patient stated



that her hands and feet readily became numbed and blue in cold weather, but no decided symptoms of Raynaud's disease could be found. The blood examination showed nothing distinctive. The red blood corpuscles numbered 4,120,000 per cub. mm., the leucocytes 8,437, and the hæmoglobin was 80 per cent. (male standard).

The differential leucocyte count was as follows :—

Polymorphonuclear cells	...	...	74 per cent.
Small lymphocytes	...	...	21 "
Large lymphocytes	...	...	3 "
Coarsely granular eosinophile corpuscles			2 "

*Filaria* embryos were searched for in both night and day specimens of blood, and none were found. The patient, it may be mentioned, had not been out of England, so that filariasis seemed out of the question. The blood coagulation time was approximately normal.

The eye condition—chronic blepharitis and conjunctivitis—has already been alluded to.

The thyroid gland could be felt in the neck, and it seemed to be natural.

The patient's height was five feet three inches.

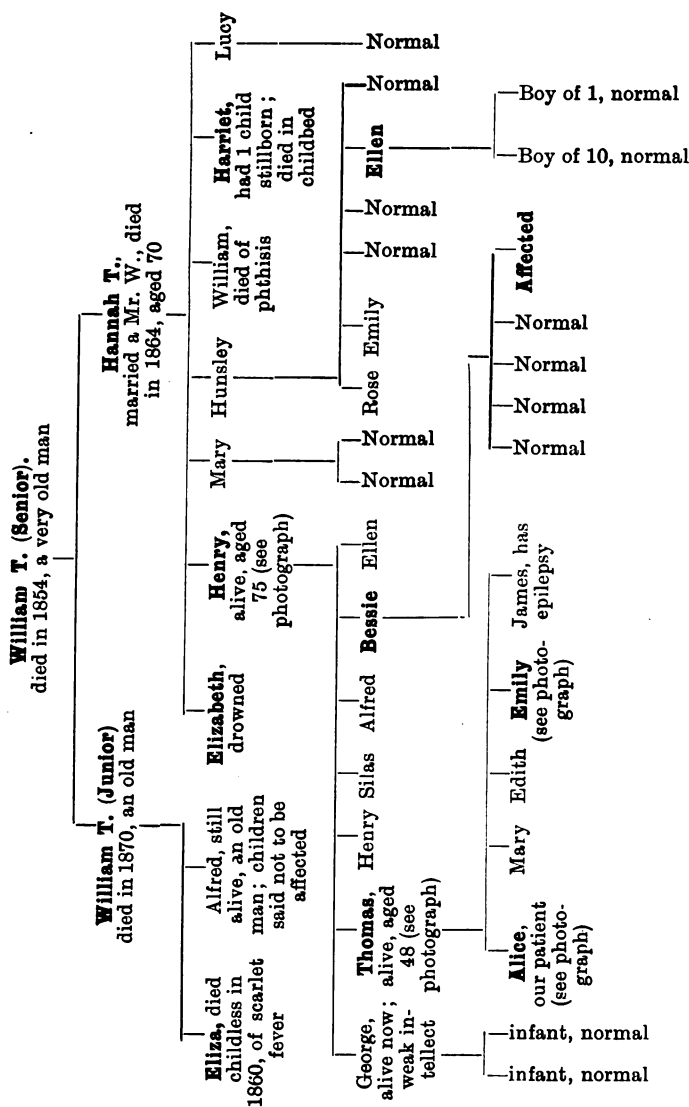
The diagnosis of this patient's condition was much simplified when the family history was obtained. There were thirteen similar cases in five generations. When an individual had the hereditary complaint we summarize this by merely stating that there were "swollen legs," without going into detail in each case. The swollen legs, when mentioned, began young and lasted long.

The individuals whose names are printed in thick type had, or have, the family complaint of "swollen legs," mostly with "acute attacks" as well.

#### *First Case traced.*

GENERATION 1.—The first member of the family of whom we had any account was William T. It is reported that he "had very swollen legs all his life," but no further particulars are available. He died in 1854 at an advanced age.

## GENEALOGICAL TABLE OF THE FAMILY.

*Children of William T., senr.*

GENERATION 2.—William T. had two children, William and Hannah. This William was affected by “swollen legs” and “attacks.” He died in 1870. Hannah also had “swollen

legs" and "attacks." She died in 1864 when seventy years of age. She had married a Mr. W., and our patient is one of her descendants.

*Children of William T., junr.*

GENERATION 3. — William T., junior, had two children, Eliza and Alfred. Eliza had "swollen legs" and "attacks." She married, but had no children, and died in 1860 of scarlet fever. Alfred is still alive, and is quite free from the swollen-leg complaint, as are his children also, so far as we have been able to trace them.

*Children of Hannah W. (née T.).*

Hannah W., daughter of William T., senior, had the following children: Elizabeth, Henry, Mary, Hunsley, William, Harriet, and Lucy.

Elizabeth, who had "swollen legs," went to America, and is thought to have been drowned.

Henry is alive now, aged 75, a cowman by occupation. He was first troubled by his swollen legs when he was nine years old. The œdema was persistent, but was kept under control by bandages. At twenty years of age he had his first "acute attack," similar to those of our patient, and he has had many "acute attacks" since, though the last one was twenty-five years ago. He is hale and hearty, notwithstanding his age. The swelling affects the dorsum of the feet, and the legs nearly to the knee, where it stops suddenly. The accompanying photograph (Fig. 3) does not make the swelling very apparent, because the patient keeps his legs constantly bandaged, knowing what a size they get if the bandages are left off. The creases caused by the bandages show fairly well. Some months ago this man had to take some cows to the local market, and in running after them his bandages came off and could not be replaced; on returning home at night the legs, up to the knee, were a great size, but there was no opportunity of getting a photograph of them then. The vigour of the man, notwithstanding his age, is shown by the way he could run after the cows.

*Persistent Hereditary Œdema of the Legs with  
Acute Exacerbations. Milroy's Disease.*



FIG. 3.





*Persistent Hereditary Œdema of the Legs with  
Acute Exacerbations. Milroy's Disease.*

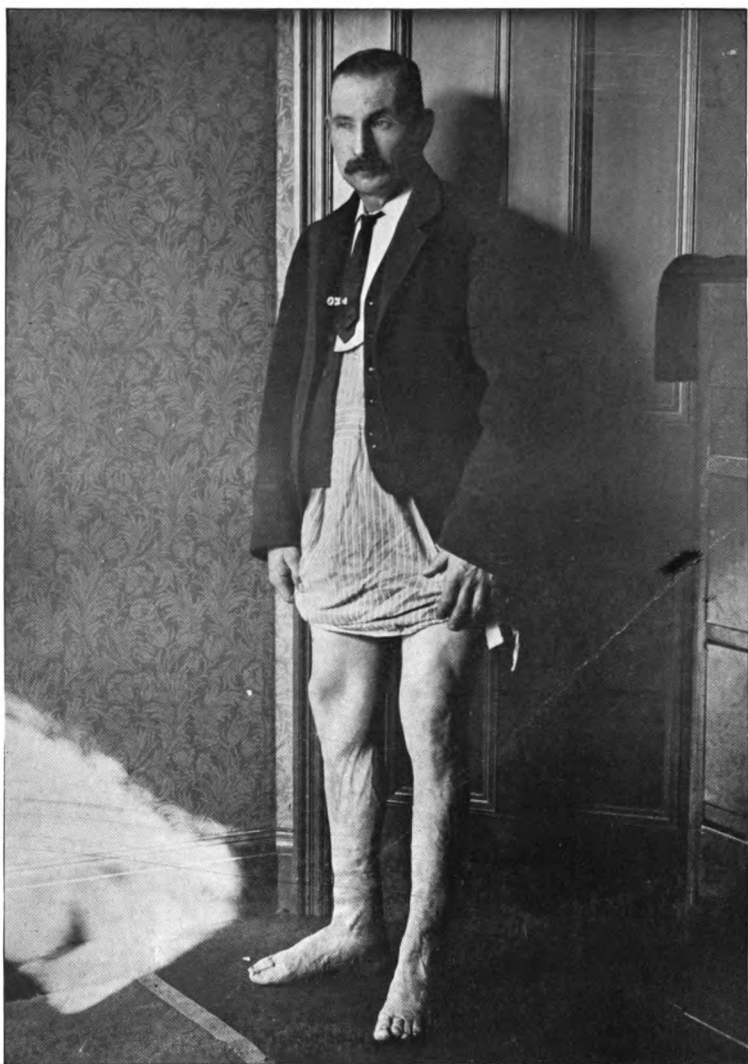


FIG. 4.

His children, George, Thomas, Henry, Silas, Alfred, Bessie, and Ellen, are mentioned again below.

Mary was normal and had two normal children.

Hunsley was herself normal, but of her six children, Ellen, Rose, Emma, and three more, one (Ellen) had the "swollen legs" and "acute attacks" (*vide infra*).

William was free from œdema, and died of phthisis, childless.

Harriet suffered from girlhood with the "swollen legs" and "acute attacks." She died in her first confinement, and the child was stillborn.

Lucy is normal, and has a normal child.

#### *Children of Henry W.*

GENERATION 4.—George W. is alive, and in good bodily health, but he is of extremely poor intellect. He is free from œdema, but he is so dull and slow that he is barely able to earn his living, and he is the butt of his fellow-workmen. He has two infant children, neither of whom has the hereditary complaint so far.

Thomas W., who is now forty-eight years of age, has the "swollen legs" to a moderate extent, and has also had the "acute attacks." His present condition does not show any better in the photograph (Fig. 4) than does that of his father, Henry, and for the same reason, namely, that the legs are kept constantly bandaged. The trouble is more marked in the right leg than it is in the left, but both legs are affected up to the knees, and not higher. The photograph was taken immediately after the removal of the bandages; it shows the creases and folds of the latter. His intellect is fairly good, but he lacks enterprise and energy; so much so that he gave up a position of trust, and took one in which the wages were less in order to escape responsibility. The swelling of the legs was first bad when he was eighteen years old. On three occasions during the last two years he has had "fits," which we have not seen, but which have been described by a person who saw one of them. About 7 p.m. he went out to his allotment, and was talking to a man, when he suddenly fell down and struggled with both arms and both



legs, and frothed at the mouth. The convulsion lasted about twenty minutes. On recovery he had no knowledge of what had happened. It is possible that the attack was epileptic. On the last occasion he was going down a ladder when the seizure came on. He fell to the bottom, and contused himself severely. He says that for two days before a "fit" comes on he has "a catch in his voice."

We have notes of two "acute attacks" in his legs, similar to those we have described in his daughter Alice. On November 10th, 1904, at 11 a.m., when at his work, he was suddenly seized with pain in his right groin. This was immediately followed by shivering. He next had pains in the back and hip. On examination there was a large painful swelling at the back of the right thigh, and the right knee was red, painful, and a little swollen. There were no varicose veins, though some of the veins looked unduly full. The upper part of the leg was normal. The lower third of the leg, the ankle, and the foot were swollen, red, and painful. Next day, the patient's temperature was 100° F., the pulse rate 100, and the respiration rate 23 per minute. There was no abnormality in the cardiac sounds; indeed, all the visceral systems seemed natural. The thigh was now less swollen, and the knee both less swollen and less red. The foot and ankle were still red and swollen, but no longer painful or tender. On November 12th, the temperature was 100.2° F., the pulse rate 90, and the respiration rate 24 per minute. Herpes had now developed on the lips and nose. The swelling of the thigh had almost gone, the knee seemed normal, and the swelling of the foot and ankle was less, and could be pitted on pressure. The redness had spread higher up the leg. On November 13th, his temperature was 99° F., his pulse rate 80, and his respiration rate 20 per minute. There was an area of redness over Scarpa's triangle on the right side, extending thence down the course of the femoral vessels and round to the popliteal space. On November 14th, the temperature had fallen to normal. The redness above the knee had all gone, except for a little at the upper part of Scarpa's triangle. The foot and leg were less swollen and less red. The next day the patient had

returned to his normal state of œdema, the "acute attack" having lasted four days, and having got well spontaneously, without leaving additional œdema behind it.

The second "acute attack" that has been watched began on May 31st, 1907. On leaving work at 6 p.m. he began to shiver, and on the way home he vomited. The shivering continued until 8 p.m., when he became very hot. His right leg, which had been aching since 4 p.m., began to swell worse at 8 p.m. Next morning his temperature was 103° F., and his pulse rate 108 per minute. The right leg was hot, more swollen than usual, and painful up to the upper border of the patella. Two days later, June 3rd, the temperature was 98° F., the pulse rate 78 per minute, the pain in the leg was gone, and the swelling was almost back to its usual amount.

These attacks are all of the same character, and as transient as they are severe for the time being.

Henry was himself normal. His descendants, if any, are not known.

Silas has no swollen legs. He had convulsions in infancy. He is slow in speech and movement, but healthy.

Alfred is normal.

Bessie began to have "swollen legs" when nine years old, and the swelling steadily increased till it reached the hips, as in our own patient. She also had several of the "acute attacks," but we have not been able to get any good account of them. She married, took to drink, and died in 1901, leaving five children, of whom one, a girl, has the "swollen legs" already. The children are in Egypt, and we have not been able to obtain further particulars of them.

Ellen is normal.

*The children of Mary W.*

Mary, the daughter of Hannah W., had two children, both of whom were free from the leg trouble.

*The children of Hunsley W.*

Hunsley, the daughter of Hannah W., had six children. Of these, Rose, Emily, and three others were all normal.

Ellen suffers both from the "swollen legs" and from the "acute attacks"; we have been allowed to examine her by kind permission of her medical attendant, Dr. Mead. She is now thirty-nine. Up to twenty-one years of age she was perfectly healthy, and then, apparently without cause, her legs began to be affected by the family complaint. As far as she can remember, the trouble was first noticed at the level of the knees and thence very gradually spread down to the feet and toes. Her first "acute attack" was when she was thirty-six, fifteen years after the seemingly causeless œdema began. The "acute attacks," though so long delayed in their first onset, are now very frequent, the longest interval between them having been three months, except during her last pregnancy, when she had none. Both legs have been attacked; on one occasion the left leg was seized before the right had quite recovered, but otherwise each "acute attack" has been strictly unilateral. She herself says they come on either just before or just after the monthly period. They begin with a desire to yawn and stretch repeatedly, after which there is a shivering fit and intense pain in the groin. The shivering lasts about fifteen minutes, the hands go blue, and the leg goes red, hot, and more swollen than its average. She has to stop in bed for three days, after which she is able to get about again, though not really well for a day or two longer.

Her present condition is as follows: the toes are swollen on their dorsal aspect; there is a deep tranverse sulcus marking the site of the metatarso-phalangeal joints; the plantar surfaces of the feet are almost normal, but the dorsum is swollen and rounded with a deep sulcus over the anterior aspect of the ankle joint; the calves are uniformly swollen, notwithstanding constant bandaging; the patellæ and the outlines of the bones at the knees cannot be felt; the thighs are much enlarged, the swelling extending as high as Poupart's ligament on both sides and there suddenly ceasing. The vulva is not involved. There are no ulcers nor sore places. The patient unfortunately refuses to be photographed, and we regret this most particularly, because she exhibits the condition much better than do any of the other cases we have photographed, except Alice W. herself.



*Persistent Hereditary Edema of the Legs with  
Acute Exacerbations. Milroy's Disease.*



FIG. 5.

Measurements of Ellen's legs, taken September 17th, 1907, immediately after removal of the bandages she always wears, are as follows:—

*Maximum circumference measurements.*

			Right leg.	Left leg.
Instep	...	...	9 $\frac{1}{8}$ inches	9 $\frac{7}{8}$ inches.
Calf	...	...	17 $\frac{1}{2}$ "	17 "
Knee-cap	...	...	16 $\frac{1}{2}$ "	17 "
Middle of Thigh	...	...	19 $\frac{1}{2}$ "	20 $\frac{1}{4}$ "

The patient's height is five feet and a half inch.

William and Harriett, children of Hannah W., died childless.

*The children of Lucy.*

Lucy, daughter of Hannah W., has one child, who is still young; it has so far escaped from the "swollen leg" complaint.

*The children of George W.*

GENERATION 5. These are two infants who, as yet at any rate, show no tendency to swollen legs.

*The children of Thomas W.*

Thomas W. has five children, two of whom have the complaint.

Alice, aged 18, is the patient whom this paper centres round, and whose condition has been fully described above.

Mary, the next younger, is at present normal.

Edith, the next younger, is at present normal.

Emily is now twelve years old, and has begun to develop the swollen legs. Their condition is not as yet very bad, but they have to be kept constantly bandaged or they would swell out of bounds. The accompanying photograph (Fig. 5) shows very clearly the depressions produced in the œdema by her boot. The swelling is symmetrical, does not affect the feet so much as it does the legs, and stops suddenly just below the knees. The general health and activity are good. No cause could be

assigned for the œdema. Emily has, like her father and sister, been subject to what we have called "acute attacks," one of which was observed. It began on July 6th, 1906, at 6 a.m., with a shivering fit which lasted till 8 a.m. She vomited, complained of headache, and had a pain along the outer aspect of the right thigh. At 9 a.m. her temperature was 101° F. At 4 p.m. her temperature was 108·2° F., and her pulse rate 116 per minute. Her visceral symptoms all seemed natural. Her right foot was red and swollen. An irregular circle of redness, about nine inches wide in front and two inches wide behind, surrounded the right calf, and felt much hotter to the touch than did the surrounding skin. It did not project like erysipelas. The veins on the thigh and leg became unduly visible, but they were not prominent. A single lymphatic gland, not very big, could be palpated in the groin, and little pellet-like nodules could be felt in the skin around the reddened area. Next day, July 7th, the temperature was 102° F., and the pulse rate 96 per minute. The redness of the right leg was more general, the foot more swollen, and a red patch was present over the patella. The patient was very sick, being unable to keep even water in her stomach. On July 8th the temperature was 98·4° F.; the swelling and redness were still present, but considerably diminished. On July 9th the leg and foot were still swollen and faintly red, but not painful. The red patch that had been on the calf was surrounded by minute raised spots, bright red in colour, discrete, and rounded. On July 10th the leg began to ache during the afternoon; during the night it "burned," and on July 11th it was red and swollen as at first. The temperature of the reddened skin was 99·4° F. when taken with an ordinary clinical thermometer under a pad of wool, whereas that of the left leg taken in the same way was 95·4° F.; the mouth temperature at the same time was 102° F. On July 12th the mouth temperature was 100° F. By July 16th the redness and pain has almost gone; the swelling persisted, and, as is shown in the photograph, it is present about equally in each leg. A similar "acute attack" occurred on the left side, beginning on July 18th, 1907.

James, the youngest, is as yet normal as regards his legs, but he is subject to epileptic fits.

*The children of Bessie.*

Bessie, the daughter of Thomas W., had five children. These are all in Egypt, and cannot be seen by us personally. We have made inquiries, and we learn that four of the five are normal, but that the fifth already has the "swollen legs," which began without apparent cause, and seem to be running the same course as have those of the other members of the family who have been affected.

*The children of Ellen, the daughter of Hunsley W.*

Ellen has two children, both boys, one aged ten years, the other twelve months; both of these show no tendency to "swollen legs" at present, but it is too early to say that they are really free from the complaint.

The relationships between the different individuals we have been able to trace is shown in the Genealogical Tree, p. 13.

The diagnosis in the case of our patient, Alice W., would have been difficult if the family history had not been so definite; but with that it was clear that the condition was very similar to, if not identical with, that described at length by Milroy, in America, in 1892, as "An undescribed variety of Hereditary Œdema," and in France, in 1898 and later years, by Henry Meige as "Trophœdème Chronique Héréditaire." The only account that we have found of any similar family in England is that of H. D. Rolleston, in his paper upon "Persistent Hereditary Œdema of the Lower Limbs," in 1902. The literature contains fairly numerous isolated cases, but the fullest accounts of the condition are given by the authors just mentioned.

Milroy's cases are the most numerous—twenty-two affected persons amongst ninety-seven individuals in six generations. Meige's cases numbered eight affected persons in four generations, Rolleston's cases numbered three in two generations. Our own number thirteen out of forty-two persons traced in five generations. In France, the condition is termed Meige's disease. If



priority of description is to count for anything, and if the disease is to be named after a person, it should be called Milroy's disease. If no person's name is to be included in the title, it may be well styled "persistent hereditary œdema of the lower limbs," after Rolleston, until its pathology is better known, and a shorter scientific name for it can be devised.

### *The Differential Diagnosis.*

It will scarcely be necessary to go into the differential diagnosis in great detail. This has already been done by Meige, in a very able manner. Suffice it to say, that cardiac, pulmonary, renal, and hæmic causes for the œdema can be rapidly excluded, and that myxœdema, though possibly a real difficulty in some cases, can usually be excluded by the normal conditions of the rest of the body, by the presence of the thyroid gland, by the fact that the œdema is real and not merely apparent, and by the fact that the administration of thyroid extract does not ameliorate the condition of the legs.

It soon becomes clear that there is almost certainly a local cause for the œdema, and the three chief local causes that might produce a similar condition would seem to be:—

1. Venous obstruction or thrombosis.
2. Lymphatic obstruction.
3. Errors in the behaviour of the blood vessels or lymphatics, without there being any actual obstruction to them—vasomotor neurosis.

### *The relation between the "swollen legs" and the "acute attacks."*

Before we can go further with the discussion of the last paragraph, it will be necessary to say a word or two as to the relation between the "swollen legs" and the "acute attacks," which so many of the above patients have had. If an "acute attack" were always the first thing, then it would be very difficult to exclude venous thrombosis or lymphatic obstruction, secondary to inflammation, as a cause for the œdema. The remarkable thing is, that the "swollen legs" have come on gradually, without any assignable cause; and in one case the "swollen legs" had

been present for five-and-twenty years before any "acute attack" occurred at all.

It seems clear, therefore, that the "acute attacks" are either accidents, or at most concomitants, rather than essential factors in the œdema. We do not know what is the nature of the "acute attack," but we shall discuss it again when we mention angio-neurotic œdema; we are bound to admit that, though possibly a "vasomotor phenomenon," each "acute attack" bears some resemblance to a temporary microbial infection comparable with erysipelas. The rigor, the pyrexia, the painfulness of the part affected, the vomiting that may occur at the same time, all suggest microbial infection. On the other hand, the attacks are remarkably transient, lasting but three or four days; they pass away spontaneously without any particular treatment, and they seem to be quite free from danger, for not one of the patients has died of septicæmia, even when the "acute attacks" have been constantly repeated. Upon the whole, we are inclined to think that the "acute attacks" are not due to sepsis, or, at least, that they are not primarily due to micro-organisms, but rather to vasomotor troubles. Be this as it may, our point is that the œdema precedes any "acute attack," and may precede it by as much as twenty-five years. There seems, therefore, to be none of the ordinary causes of venous thrombosis or of lymphatic obstruction underlying the œdema.

*Other reasons for excluding venous thrombosis or lymphatic obstruction.*

Besides the above, there are other reasons for excluding venous thrombosis or lymphatic obstruction as the original cause for the œdema. First, there is the distribution of the swelling. The cases recorded by Meige agree with ours in the fact that the œdema receives a sudden limitation at the level of a joint. In Alice W. it for some time ceased at the ankle; we have several cases in which the œdema stops at the knee, and several others in which it stops at the hip or groin. The œdema does not stop gradually, moreover, but suddenly, and does not involve the vulva or the abdominal wall, although it may become extreme

immediately one passes down over Poupart's ligament. This would be difficult of explanation if the obstruction were in the pelvis; and, when the swelling is bilateral, it is difficult to understand how any obstructive lesion in veins or lymphatics should be well-marked right up to Poupart's ligament on both sides and yet not extend into the pelvis in any single one of the patients recorded by Milroy, Meige, Rolleston, ourselves, or any of the observers we can find. Venous obstruction seems unlikely on this further ground, namely, that the circulation in the affected legs seems to be quite good; a patient over seventy who has had the œdema all his life has been able to run about after cows, so that his muscles must have been well supplied with blood. Visible distension of the veins in the legs is a rarity in the cases. The feet are not unduly cold. It is conceivable that there might be some congenital abnormality in the structure of the lymphatics from Poupart's ligament downwards; but against this view are the facts that it may be twenty years before the œdema sets in, that when it does set in it may be restricted to the level of the knee for years before it reaches to Poupart's ligament, and that when it spreads at all it spreads at one time the full distance from one joint level to the level of the next joint above (Meige). Upon the whole, therefore, although it cannot be called a very satisfactory explanation, we think, with Milroy, Meige, and others, that the œdema in these cases is secondary, not to gross structural changes in the blood-vessels or lymphatics, but to an error in the functions of these vessels, presumably, or at least possibly, resulting from erroneous functions in the nerves supplying them—in other words, we think the condition is primarily a *vasomotor neurosis*.

*The relation of these cases to those of angioneurotic œdema  
and of other vasomotor neuroses.*

There are three well-known conditions in which vasomotor neurosis is generally held to be at the root of the affection. These are Raynaud's disease, factitious urticaria, and angioneurotic œdema.

These are so distinct in their objective manifestations that it would not be at all surprising if other, and at first sight wholly different, manifestations of vasomotor neurosis were possible. Our cases show little in common with Raynaud's disease; that is to say, they could scarcely be mistaken for cases of Raynaud's disease, although, in addition to their œdema, cold weather causes several of the patients to suffer from blueness of the hands, which to some extent resembles Raynaud's disease. Similarly, they could not be taken for cases of factitious urticaria. Nor could they, we think, be taken for a variety of angioneurotic œdema in the ordinary sense of the latter term. Nevertheless, there are distinct points at which angioneurotic œdema and our cases of Milroy's disease come close together—notably in the strongly-marked hereditary disposition, and possibly in the "acute attacks" to which many of the above patients were subject. It seems likely that Raynaud's disease, factitious urticaria, angioneurotic œdema, and Milroy's disease are related to one another pathologically, but that their objective manifestations are so well defined and so different that these different kinds of vasomotor neurosis merit distinctive names. It may be noted that, apart from the "acute attacks," our cases had absolutely painless swelling of the legs, and no general disturbances of health at all, whereas during the "acute attacks" there was considerable constitutional disorder, sometimes with marked vomiting for a short time, comparable to the colic, nausea, and vomiting often seen during exacerbations of angioneurotic œdema. So like the latter were the "acute attacks," except in so far as they were confined to the legs instead of varying in place and affecting body, face, hands, arms, or throat, that we felt very much inclined to call them definitely "angioneurotic attacks." This, however, we have refrained from doing, because we cannot bring forward absolute proof that they were angioneurotic.

*The incidence of other nervous complaints in the family.*

It is often a very difficult thing to elicit a history of insanity or fits in a family. Nevertheless it is interesting to observe that

Alice W.'s uncle George is of weak intellect and the village butt; that her father Thomas has had three "fits," which seem to have been very like epilepsy; that Silas is slow-witted; that Bessie was a dipsomaniac; that Alice herself has had an attack of garrulous mania, with delusions; and that her brother, James, a young boy, has already had many epileptic fits. A similar history of epilepsy in members of a family in which other members are subject to the trophœdema of the legs has been noted by other observers, and the point is of interest in connection with the angioneurosis that is supposed to be at the root of the trophœdema.

*The points in which our cases resemble, and the points in which they differ from, those recorded by others.*

The points in which our cases and those recorded by others closely resemble one another are as follow:—

1. The restriction of the œdema entirely to the legs.
2. The absence of any traceable cause for the œdema, general or local.
3. The strong family predisposition to the complaint.
4. The painlessness of the pale swollen legs (apart from the "acute attacks" in our cases).
5. The absence of constitutional symptoms.
6. The sharpness of limitation of the upper level of the œdema.
7. The incidence in both males and females.
8. The permanence of the œdema when once it has appeared.

There are certain points, however, in which our cases differ from those of others. Meige, for instance, lays stress upon the absence of "acute attacks," which occurred on more than one occasion in most of ours. Milroy lays stress upon the œdema being present at birth; Meige lays stress upon its appearing at puberty; in our cases not once was it actually noted at birth, and the age at which it first attracted attention was sometimes in infancy, sometimes in boyhood or girlhood before puberty, sometimes not until the teens were passed.

The fact that there are differences such as these is not to be wondered at, seeing that the cases recorded by each individual observer all belong to one family, and are, therefore, likely to resemble one another, but to differ in details from cases arising in a different family observed by some one else. Small points of difference by no means indicate differences in kind; they may well be but family variations in the same condition.

*Comparison with muscular dystrophies.*

Several observers have aptly compared this disease to that of the muscular dystrophies; the latter may be present at birth (congenital), or they may develop later (hereditary). Similarly, it seems that trophœdema of the legs may be congenital and present at birth, as in Milroy's cases, or it may be hereditary and only develop later at a constant period after birth (puberty), as in Meige's cases, or at a variable period after birth, as in ours.

*The treatment of the condition.*

Little treatment is required in the majority of the cases, beyond firm and constant bandaging of the legs. Several of our cases lived to over seventy years of age, having suffered from the complaint for sixty years or more, but having kept the swelling in check by constant bandaging.

The "acute attacks," dangerous though they look, pass away spontaneously in a few days, and all that can be done for them is to relieve the pain by putting the patient to bed and applying anodynes to the affected part.

Our own patient's condition had passed all bounds so far as keeping the œdema in check by bandaging was concerned, and all treatment for the condition was a failure as regards ameliorating it. The œdema always diminished to some extent with rest in bed, and firm bandaging was a relief to the patient when she was able to get up after such rest. Medicinal treatment of various kinds was tried in vain—thyroid extract, diuretics, purgatives, potassium iodide, mercury, intestinal antiseptics, bromides, valerianate of zinc, and so forth. None made the

least impression on the leg condition. One observer has recorded benefit in one case from electrical treatment, and one or two have recommended massage. The latter may alleviate the œdema temporarily, but when the swelling has got beyond bounds, as in the case of Alice W., it seems next to impossible to restore the normal conditions again. The important point seems to be to recognise the nature of the trouble early, and to keep the legs bandaged constantly from the first, so that no large increase in the œdema can occur. It may then be held in check for a great many years, as may well be seen in the photograph of the two men. These two know full well what would happen if the bandages were long off whilst they were upright, and they will not leave the bandages off at all; otherwise the photographs of them would show a great deal more œdema than they do.

*The effects of pregnancy on the condition.*

Several female members of the family married when the trophœdema was well advanced. It might have been thought that the œdema of the legs would certainly have been made materially worse by pregnancy. This has not been the case, and in one instance, in which the "acute attacks" had been frequent previously, they were in complete abeyance throughout a pregnancy. The fact that the leg condition is not made materially worse by pregnancy may, perhaps, be an additional argument against lymphatic or venous obstruction being its cause, and, therefore, indirectly in favour of the angioneurotic view.

*Transmission by an unaffected mother.*

It is a point that will, perhaps, interest those who pay attention to the family transmission of peculiarities that Hunsley, the daughter of a woman who had the family complaint, was not herself affected, but transmitted the trouble to her daughter Ellen. If one had the opportunity it would be interesting to see whether any of Ellen's children, escaping the trouble themselves, will one day have children who are affected.

*Conclusion.*

The family of which we have given an account seems comparable, with minor differences, to those described by Milroy, Meige, Rolleston, and others. The chief points in the malady from which certain members of the family suffered—thirteen out of forty-two individuals in five generations—are summarized on pages 26 and 27, the most obvious being painless persistent œdema of one or both legs, arising apparently without cause, and apart from any constitutional ill-health. The malady has received various names, of which we select Persistent Hereditary Œdema of the Legs, or Milroy's Disease. The disease affects both males and females, and is not itself inimical to life; though in some cases the œdema becomes so like elephantiasis that locomotion is greatly impeded, or even rendered almost impossible, as in the case of Alice W.\* There is often a history of epilepsy or other nervous disorder in the same family. Our cases, unlike those of some observers, were subject to what we have described as "acute attacks," many of which we have described in detail. The condition differs objectively very much from Raynaud's disease, factitious urticaria, and angioneurotic œdema, but we think that there is evidence that, underlying both these three conditions and our cases of Milroy's disease, there is a common pathology, namely, that of a vasomotor neurosis.

\* Alice is now, August, 1908, quite unable to walk.

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## DESCRIPTION OF PLATES.

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- FIG. 1. Alice, Persistent Hereditary Œdema of the legs.
- FIG. 2. Alice, Persistent Hereditary Œdema of the legs.
- FIG. 3. Henry, grandfather of Alice. The leg-bandages have just been removed. The œdema has been present for sixty-six years.
- FIG. 4. Thomas, father of Alice. The leg-bandages have just been removed. The œdema has been present for thirty years.
- FIG. 5. Emily, sister of Alice. Persistent Hereditary Œdema of the legs is beginning to develop.



# CEREBRAL CYST IN A MAN WITH AN ABNORMALLY SITUATED ROLANDIC FISSURE SUCCESSFULLY REMOVED BY OPERATION.

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AND

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HERBERT P., a hawker, aged 29, an American by birth, was admitted into Guy's Hospital under the care of Dr. Hertz, on August 8th, 1907. For ten years he had suffered from Jacksonian epilepsy. The fits were always preceded by a tingling sensation in the left hand and arm, which generally lasted sufficiently long for the patient to reach a place of safety before the attack began. The convulsions, which were first tonic and then clonic, always commenced in the left hand; they spread up the arm and often, but not always, affected the left leg. On rare occasions movements of the right side of the body followed those of the left; when this happened, consciousness was generally lost, though in the milder attacks the patient always remained perfectly conscious. Neither involuntary defæcation nor micturition ever occurred during a fit. The duration of the attacks varied between a few seconds and two minutes. On an average the patient had had one fit a week, but during the year previous to

his admission the number had greatly increased, and latterly as many as six had occurred in a day. The patient had never been troubled with sickness, headache or giddiness.

In 1898, the patient was in a Boston hospital, where he was trephined over the right Rolandic region in the hope of finding the cause of his epilepsy. Nothing abnormal was discovered, and the patient gained no relief from the operation. In 1904, directly after his arrival in England, he had a very severe fit, accompanied by unconsciousness. He was taken to the local hospital, where the association of left-sided convulsions, with a depression in the skull on the right side, led to a diagnosis of depressed fracture being made. An operation was performed, but the depression was found to be due to the previous trephining, as the bone had not been replaced, so nothing further was done.

On admission, the patient's general health was found to be good. His heart and lungs were normal, and his urine contained neither albumin nor sugar. He was rather excitable, but he was otherwise mentally normal. His pupils reacted to light and accommodation and were equal in size. The optic discs were normal. There was some weakness of the left arm, which had developed gradually since the fits had become more frequent, but the leg was of normal strength. The superficial reflexes and tendon phenomena were normal. Sensation was normal, except on the left forearm and hand, where there was impaired sensibility to touch, temperature and pain.

The fits became steadily more frequent in spite of the administration of bromides and morphia. Ten days after admission the patient had over a hundred fits in one day. The majority were still confined to the left arm, but some were bilateral and accompanied by respiratory spasm and unconsciousness. The weakness of the arm developed into complete paralysis, and the left leg also showed a diminution in strength. The convulsions were so frequent that an extensor plantar reflex could be almost always elicited on both sides, the tendon reflexes became exaggerated, and ankle clonus developed on both sides. The patient became much depressed. He said that he would gladly submit to any operation, even if it resulted in

complete hemiplegia, so long as he could be relieved from the incessant fits.

Seeing that the operation in Boston was performed at a time prior to the publication, in 1902 and 1904, of the investigations of Sherrington and Grünbaum, which demonstrated that the motor area is entirely anterior to the Rolandic fissure, it was hoped that the cause of the Jacksonian epilepsy might be found anterior to the part of the brain previously explored, as the centre of the trephine hole was found to be slightly behind the probable position of the Rolandic fissure as determined by two different methods, the results obtained by which corresponded accurately with each other. The operation was performed at 8 p.m., on August 21st, by Mr. Rowlands. A large flap of the scalp was turned down over the zygomatic arch, exposing the gap in the skull and a wide margin of bone around it. The gap was about two and a half inches long and one and three-quarter inches broad, with its long axis running downwards and forwards. An inch more bone was removed from the anterior margin. The dura mater was opened and carefully raised from the brain to which it was adherent at the site of the former operation.

As nothing obviously abnormal could be seen, an attempt was made to discover the motor area for the hand by faradisation of the cortex. A large electrode was applied to the back of the neck, and a sterilised electrode of the kind employed for intralaryngeal treatment was used for the cerebral cortex. When the electrode was applied to the exposed part of the brain, faradisation gave rise to a movement of the head and eyes towards the opposite side. It is now known that this movement is produced by stimulation of the central part of the middle frontal convolution. It appeared probable, therefore, that the arm area would be found further back. No movement was produced by stimulation of the part of the brain which had been exposed by the operation done in Boston. Some more bone was therefore removed from the postero-superior margin of the original aperture. On now stimulating the postero-superior part of the exposed brain the index finger of the left hand twitched. The point stimulated must have been in the ascending

frontal convolution, although it was situated about two inches behind the position indicated by the surface marking, the latter being occupied by the area for the head and eyes, and presumably therefore by the middle frontal convolution.

Investigation of the hand area thus discovered revealed the presence of a small, very thin-walled cyst. It was about five-eighths of an inch in diameter and contained clear colourless fluid. It was situated in one of the small fissures in the neighbourhood of the hand area, upon which it had exerted pressure. The compressed convolutions were œdematous. The fluid escaped from the cyst, the wall of which was then completely removed without difficulty.

After the operation there was considerable venous hæmorrhage, which could only be controlled by the application of a gauze plug, which was renewed twice during the next two days, after which the bleeding ceased. During the three days which followed the operation there were no fits, the strength of the left arm increased, the extensor plantar reflex, ankle-clonus, and exaggeration of the knee-jerks disappeared, and the patient became more cheerful.

On August 25th, he began to complain of headache. His temperature rose, and his left arm and leg became increasingly weak. There was a slight discharge from the wound. In the course of the next three days the left arm and leg became completely paralysed, and the left side of the face became paretic, but there were no fits. The left knee-jerk became exaggerated, and the ankle-clonus and extensor plantar reflex reappeared on the same side. A small cerebral hernia slowly developed.

On September 2nd, the hernia, which was now the size of an orange, was explored by means of a needle, but no collection of pus was found. An ounce and a half of clear fluid, under moderate pressure, was then withdrawn by lumbar puncture, without, however, producing any marked change in the size of the cerebral hernia. The *streptococcus longus* was cultivated from the discharge from the wound. The patient now became very drowsy, and his temperature remained between 101° and 103°. The scalp and skin of the forehead and eyelid of the right

side became œdematous. The infection of the wound was secondary in origin, and must have spread along the track of the plug which, unfortunately, had to be used to arrest the rather severe hæmorrhage which took place from one of the thin-walled superior cerebral veins close to the superior longitudinal sinus under the cover of bone. The patient though drowsy was sometimes violent, and removed his dressings on several occasions in the early days after the operation.

On September 4th, and again two days later, 10 cc. of anti-streptococcic serum were injected. The temperature at once fell to normal, and did not rise again, and the œdema soon disappeared. A fortnight later the patient was quite cheerful, and the drowsiness had disappeared; but there was no change in the size of the cerebral hernia, and the paralysis showed no signs of improvement.

After the middle of September, however, the cerebral hernia became steadily smaller, and the power of the left side of the body gradually returned. On October 1st, the patient began to walk; the paralysis of the tongue and face had disappeared, and the arm was much stronger. The hernia cerebri was quite small. When he was discharged, on December 2nd, 1907, the hernia had completely disappeared, and the operation wound was healed. There was no longer any paralysis of the face or tongue, but there was some weakness of the extensors of the wrist. The patient could walk quite well, but his left leg was still somewhat spastic, and an extensor plantar reflex was present on the same side.

The patient was again seen about December 20th. He looked and felt quite well, and had had no fits since the operation, four months before. Shortly afterwards he was seen hawking cough lozenges in the streets of London.

On August 21st, 1908, the anniversary of the operation, a letter was received from the patient, who is now living in Brighton. He says that he has had no more fits; he has never felt so well and his life is now a source of pleasure to him. He has married, and has put on three stone in weight. He does a little hawking and poem writing, and lectures on the beach on the five Senses



of Humanity. He concludes by writing: "I intend to Rhyme some verses on the great Surgical sensation at Guy's if you will kindly favour me with the notes for a short time."

We are indebted to Mr. Steinbach for the notes upon which the above account is based.

From a study of this case the following conclusions may be drawn:—

1. A simple serous cyst situated in the motor area of the cerebral cortex may, by the pressure it exerts, produce very serious Jacksonian epilepsy for a period of many years without necessarily growing beyond a very small size.

2. The Jacksonian epilepsy may be completely cured by removal of the cyst, even after it has been present for as long as nine years.

3. The generally accepted methods for marking the cerebral fissures on the scalp are not always correct. In this case, the arm area in the ascending frontal convolution was situated about two inches further back than the external measurements, made by two independent methods, led us to expect.

4. Faradic stimulation of the cerebral cortex may be of the greatest value as a help in the localisation of cerebral tumours or cysts, which are not discovered by simple inspection.

5. The faradic stimulation of the cortex in this case confirmed the few observations already made on man, which show that the area for conjugate movements of the head and eyes is situated, as Sherrington and Grünbaum discovered was the case in anthropoid apes, considerably in front of the arm area, and probably therefore in the middle frontal convolution.

# GASTRO-ENTEROSTOMY IN GASTRIC ULCERATION.\*

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By H. C. CAMERON, M.B.

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TWENTY-SIX years ago Wölffler, of Vienna, carrying out Nicoladoni's suggestion, performed for the first time the operation of gastro-jejunostomy. At the present time it has become one of the common operations of surgery, and is the method adopted almost as a matter of course in the relief of obstruction, whether simple or malignant, at the pyloric outlet of the stomach. In many such cases the success has been very striking. It is quite a common thing to meet with cases in which the operation has been the means not only of removing intolerable pain, not only of prolonging life, but of restoring the patient to apparently unimpaired health and activity. Emboldened by such successes, and reassured by statistics which show a mortality dwindling almost to insignificance, surgeons have, perhaps, been only too ready to enlarge the scope of its application. In cases where there exists no obstruction to the pyloric outlet, and no dilatation of the stomach, in acute gastric pain, where the possibility of gastric ulceration has been considered but there is no certainty, in hæmatemesis, whether due to ulceration or not, and in ulceration of the duodenum, the operation is now frequently performed, and it is claimed that these various conditions have

\* The substance of this paper formed part of a Thesis for the M.D. Degree of the University of Cambridge. The expenses of the work were defrayed by a grant to Dr. Pembrey from the Royal Society.

been either cured or relieved. Besides, it is argued, the danger is so little. Intestinal obstruction, whether by kinking of the gut itself or by accidents with button or bobbin, has become, with improved methods, a comparatively rare complication, while the chance of peptic jejunal ulceration is so remote as to be negligible.

Nor can it be urged against it that the operation is followed by any very obvious impairment of digestion or absorption of food. In the light of recent advances in our knowledge of gastric and pancreatic digestion this is, perhaps, not a little surprising. In physiology no investigations have proved more fruitful than those of Pawlow and his fellow-workers in St. Petersburg, and of Bayliss and Starling in London. Ten years ago, when gastro-enterostomy had already become a frequent method of procedure, matters were very different. At that time we had, indeed, some knowledge of the changes which the food underwent in the process of digestion. The special activities of each gland were known to us; we were able to analyse and record the nature and composition of its secretion; but of the stimulus which called forth these activities, and which induced this secretion, we were profoundly ignorant. Since that time the work of Pawlow, and of Bayliss and Starling, has given to us a new conception—the continuity of the process of digestion. Pancreatic digestion is no longer regarded merely as following gastric digestion, and in no sense occasioned by it or modified by it. With the knowledge that the adequate secretion of pancreatic juice is intimately dependent upon the changes which the food has already undergone, that is to say, upon gastric activity, we may very well expect to find that the mutilation entailed by “short-circuiting” the duodenum has impaired the stability of the whole process.

Experiments on metabolism after gastro-enterostomy have been carried out by at least two observers. Joslin,<sup>1</sup> working in Ewald's laboratory, published the results of observations upon two patients with gastro-jejunosomy which had been performed for malignant disease.

CASE 1.—A woman, æt. 45, from whom two-thirds of the stomach had been removed for carcinoma. The ends of the

duodenum and stomach were closed and gastro-jejunostomy performed. Her metabolism on a mixed diet was investigated, with the following result :—

	Absorbed.	Unabsorbed.
	Per cent.	Per cent.
Fat ... ..	81·3	18·7
Nitrogen... ..	87·4	12·6

CASE 2.—A male upon whom gastro-jejunostomy had been performed for carcinoma :—

	Absorbed.	Unabsorbed.
	Per cent.	Per cent.
Fat ... ..	68·79	31·21
Nitrogen... ..	80·05	19·95

In the Hunterian Lectures on gastro-jejunostomy, delivered at the Royal College of Surgeons in 1906, Paterson<sup>2</sup> criticises these observations, pointing out that their value is diminished by the circumstance that the patients were suffering from cancer. He himself repeated the experiments in four non-malignant cases.

Few details as to the experiments are given, nor is it stated, in all cases, whether or not the pylorus was obstructed. The patients were fed upon a mixed diet.

	Period since operation.	Fat absorbed.	Fat unabsorbed.	Nitrogen absorbed.	Nitrogen unabsorbed.
		Per cent.	Per cent.	Per cent.	Per cent.
Case 1 ...	5 months	92·3	7·7	91·0	9·0
Case 2 ...	7 months	92·5	7·5	90·5	9·5
Case 3 ...	24 months	92·7	7·3	92·1	7·9
Case 4 ...	2 months	94·7	5·3	92·7	7·3

These figures show that in non-malignant cases the digestion and absorption of nitrogen and fat is impaired only to a very slight extent.

More recently Paterson states that he has found little diminution in the power of digesting fat in four patients with gastro-jejunostomy who were placed upon a *milk* diet. The fat absorption is stated to have been on an average only 1·17 per cent. below the normal. The amount of milk given is not mentioned. It will be seen that this is in opposition to my own results.

But the question is not one of real practical interest. Surgeons are rightly in the habit of estimating the success or failure of their own work by the measure of their own personal experience. The knowledge that an infant upon whom gastro-enterostomy has been performed may grow up healthy and vigorous, the evidence of the increasing weight of patients upon whom they themselves have performed gastro-enterostomy, will far outweigh the results of such experiments however indubitable and consistent they may be.

At the same time, it is certain that some modification in the process of digestion must result from so radical an operation as that of gastro-enterostomy, and merely to prove that in these patients the absorption of fat or proteid is sufficient and complete does not imply that there is no change in that process, nor is it wise to neglect altogether the study of the digestion of these patients, lest we miss thereby evidence of significance for what is still hard to understand.

We must conclude, then, that neither the difficulty of the operation, nor the subsequent derangement of digestion and absorption, is such as to deter the surgeon from recommending the operation in suitable cases. If we leave on one side the vexed question as to whether the operation is a wise procedure in cases of violent gastric hæmorrhage, the difficulty of deciding as to what cases are suitable is not great. Everyone is agreed as to its propriety in obstruction of the pylorus, whether simple or malignant, and opinion is also in its favour as the operation which is most likely to do good in cases of long-standing gastric ulceration which have resisted all medical treatment. But in this statement a difficulty becomes apparent. How are we to explain the benefit conferred alike in circumstances so widely

different? In the numerous series of gastro-enterostomies published by different surgeons, there is no hint that the procedure differs in the slightest in the two groups of cases. It was in an attempt to answer this question that the experiments described below were undertaken.

In the first place, the course of the food after gastro-enterostomy, both in cases where the pylorus was obstructed and in cases where there was no obstruction, must be determined. In the former case, *i.e.*, with an obstructed pylorus, there can be no doubt that the food leaves by the new opening. When there is no obstruction to the outlet, it is in the highest degree improbable that the food deviates from the normal course.

Cannon,<sup>8</sup> in cats upon which gastro-jejunosomy had been performed, made use of the bismuth and X-ray method to prove that in these animals the food took its normal course. In attempting to confirm these observations in man, I met with the difficulty that I was never able to photograph the duodenum nor even to identify it upon the screen with sufficient certainty.

Clinical observation, however, strongly confirms Cannon's conclusions. Thus a man suffered from a duodenal fistula which could not be got to close. A gastro-jejunosomy was performed, but the sinus still remained patent. A second laparotomy was performed and the pylorus ligatured, with the result that the fistula healed almost immediately.

From the work of Cannon and Blake it may be concluded that no opening, however large and however placed, will divert any considerable amount of the gastric contents so long as the pylorus remains unobstructed. When there is pyloric obstruction the escape will be most free from an opening placed as near the pylorus and as much in the line of forward peristalsis as possible.

More recently Legett and Maury<sup>4</sup> have adopted another device to determine the course of food after a gastro-enterostomy. They induced a dog, which had undergone gastro-enterostomy, to swallow a bullet, wrapped in a piece of meat, to which was attached a long piece of string. The other end of the string was secured around the pterygo-maxillary ligament. Some hours later the dog was killed, and the course of the bullet could then

be traced by the string. In one instance, the bullet had left by the stoma, passed round the duodenum, through the pylorus, in the reverse direction, to the stomach. It had then left the stomach a second time, again traversed the duodenum, and again entered the stomach through the pylorus. This experiment, though of interest as showing the possibility of regurgitation through the pylorus, does not disprove the assertion of Cannon and Blake. It has been known since Beaumont's observations upon Alexis St. Martin, that contact with a solid body prevents opening of the pylorus. The bullet would, therefore, be forced, if it left the stomach at all, to do so by the artificial opening.

We must conclude that, in cases with pyloric obstruction, the food passes out by the stoma, thus altogether avoiding the duodenum, and that, in cases with no obstruction, the food takes its usual course. It would appear, therefore, that a comparison of the powers of digestion and absorption in patients of these two groups—those with gastro-enterostomy performed for pyloric obstruction, and those where it was performed without obstruction—will furnish evidence as to the importance of the duodenum in digestion. If both present an equal deterioration of powers, for the same reason it will be evident that that deterioration cannot depend upon whether the duodenum is or is not short-circuited out of the alimentary canal, but must be due to some cause common to both.

In an attempt to determine this point, the power of absorbing fat in seven patients upon whom gastro-enterostomy had been performed was examined. Cases 1 and 4 had well-marked pyloric obstruction, not malignant, and in both cases there was a largely dilated stomach. Cases 2 and 5 had no obstruction at the pylorus, but hæmatemesis and indigestion. Case 3 had a simple fibrous stenosis of the pylorus; no gastro-jejunostomy was performed, but the pylorus was removed and the ends united by direct suture. Case 6 had had a gastro-jejunostomy performed for simple fibrous pyloric stenosis eight years before. In Case 7 the pyloric half of the stomach was removed for malignant disease, the ends were closed, and a posterior gastro-jejunostomy was performed. In Cases 1, 2, and 3 the patients were fed entirely on milk; in Cases 4, 5, 6, and 7 a rich mixed diet was

given—milk, cream, butter, eggs, bread, vegetables, fish, and lean meat, with tea or coffee—and the amount of fat in this diet was estimated in the following way: The quantity of fat in the milk, cream, and butter was calculated by extracting samples of known bulk or weight with ether in a Soxhlet apparatus. The amount of fat in the eggs was calculated from tables. Only fish with a very low percentage of fat was given (cod and haddock), and care was taken to remove all visible fat from the meat. With these precautions the amount of fat taken in food other than milk, cream, butter, and eggs was neglected. In Cases 1 and 2 both the nitrogenous and the fat metabolism was investigated; in the remaining cases only the fat. Attention was especially directed to the digestion and absorption of fat, because such a study provides the best means of estimating the activity of the pancreatic juice. It is true that on a milk diet, where the fat is presented in the form of an emulsion, the gastric lipase is able to split up almost the whole of it, but on a diet in which the fat consists of butter the lipase is ineffective, and the digestion must be the work of the steapsin of the pancreatic juice. By a study of the nitrogenous digestion and absorption, the activity of the pancreas cannot be estimated, because it is impossible to separate the effect of peptic digestion from that of the trypsin. In all cases a period of at least three days was allowed to pass after the special diet had been begun. The urine and fæces were collected from the fourth day onwards. The estimation was carried on for a period of at least five days. In Cases 1, 2, and 3 the nitrogen and fat in samples of the milk supplied were estimated twice—on the first day of the experiment, and again on the sixth day; the milk for the twenty-four hours was kept in a large flask, which was shaken before any feed was drawn off, to ensure that the sample was a true representative of the whole. The nitrogen in the urine and fæces in Cases 1 and 2 was estimated every day by Kjeldahl's method. In Case 3 the patient had some incontinence of urine, so that the estimation had to be abandoned. The total fat in the fæces for five days was estimated in all cases by extracting with ether in a Soxhlet apparatus weighed samples of the dried and powdered fæces, which had been collected for five days and mixed.



Table I. (given for comparison) shows the results of similar experiments conducted by various observers upon normal persons; the last column represents the average of all cases. The diet in all was milk.

Table II., taken from Harley and Goodbody's *The Chemical Investigation of Gastric and Intestinal Diseases*, p. 133, gives similar information with regard to nitrogen absorption in normal individuals.

Cases 1, 2, and 3 in the present series gave the result shown in Table III., which may be compared with the previous tables.

TABLE I.—*The Normal Absorption of Fat on a Milk Diet.*

Amount of Food.	Grams of Fat in Food.	Grams of Fat in Fæces.	Percentage of Fat in Fæces.	Percentage of Fat absorbed.	Age and Sex.	Experimenter.
1,790 c.cm. milk...	53·7	1·50	2·8	97·2	F. 12	Camerer
2,039 c.cm. milk...	57·4	1·60	2·8	97·2	F. 10	Camerer
2,050 c.cm. milk...	79·7	5·70	7·1	92·9	M. adult	Rubner
2,200 c.cm. milk...	69·1	4·93	7·2	92·8	"	Müller
2,438 c.cm. milk...	95·1	4·66	3·3	96·7	"	Rubner
3,075 c.cm. milk...	119·9	6·70	5·6	94·4	"	Rubner
4,100 c.cm. milk...	160·0	7·40	4·6	95·4	"	Rubner
3,000 c.cm. milk...	94·2	6·57	6·9	93·1	"	Rubner
3,000 c.cm. milk...	111·8	5·65	5·1	94·9	"	Prausnitz
2,632,4 c.cm. milk	93·4	4·97	5·04	94·96		

TABLE II.—*The Normal Absorption of Nitrogen on a Milk Diet.*

Number of Cases Examined.	Milk. Pints.	Average Number of Grams of Nitrogen in Fæces.	Percentage of Nitrogen Absorbed.
6	4	0·84	93·82
4	4½	0·76	95·03
2	5	1·06	93·76

TABLE III.—Nitrogen and Fat Absorption in Cases 1, 2, and 3.

	Amount and Kind of Food per diem.	Grams of Fat in Food per diem.	Grams of Fat in Faeces per diem.	Per cent Absorbed.	Grams of Nitrogen in Food per diem.	Percentage of Nitrogen Absorbed.	Grams of Nitrogen in Urine per diem.	Weight of Dried Faeces per diem in Grams.	Age, Sex, and Operation since First Day of Experiment.	Clinical Notes.
1	1,700 c.cm. milk.	69.0	8.6	87.5	7.2	97.1	7.5	25.79	F. 40 years 20 days	Mr. Golding-Bird's case. Hæmatemesis at 23 years of age; since then constant pain in stomach; posterior gastro-jejunostomy; pylorus obstructed; stomach dilated.
2	2,885 c.cm. milk.	117.8	15.9	86.6	14.75	95.9	11.5	35.17	M. 53 years 11 days	Mr. Rowlands' case. Two and a half years' history of indigestion; hæmatemesis sixteen months before posterior gastro-jejunostomy; pylorus not obstructed; stomach not dilated.
3	1,700 c.cm. milk.	67.0	17.7	73.72	—	—	—	7.74	F. 52 years 36 days	Mr. Lane's case. History of gastric pain for years; cicatricial contraction of pylorus found; pylorus excised and ends sutured together; no gastro-jejunostomy; microscopic report, "no malignant disease."

TABLE IV.—*Absorption of Fat in Cases 4 and 5 on a Mixed Diet Rich in Fat.*

The diet consisted of butter in large amount—about 3 ozs. daily—milk, cream, eggs, cod or haddock, lean meat, bread, vegetables, and weak tea.

Amount and Kind of Food.	Grams of Fat in Food per diem.	Grams of Fat in Faeces per diem.	Percentage of Fat Absorbed.	Weight in Grams of Dried Faeces.	Age and Sex. Period between Operation and First Day of Experiment.	Clinical Notes.
4 Various	122.49	5.25	95.71	23.20	F. 43 years old. 18 days.	Dr. French's case. Operation by Mr. Rowlands. Indigestion many years. Three ulcers, one on either side of pylorus. Posterior gastro-jejunostomy. Obstructed pylorus. Dilated stomach.
5 Various	201.3	7.00	96.57	41.31	M. 41 years old. 14 days.	Mr. Lane's case. Old duodenal ulcer. Posterior gastro-jejunostomy. Pylorus not obstructed. Stomach not dilated.

TABLE V.—*Absorption of Fat in Cases 6 and 7 on a Similar Mixed Diet.*

Amount and Kind of Food.	Grams of Fat in Food per diem.	Grams of Fat in Faeces per diem.	Percentage of Fat in Faeces.	Weight in Grams of Dried Faeces per diem.	Age, Sex, and Time between Operation and First Day of Experiment.	Clinical Notes.
6 Various	126.54	8.07	6.4	35.2	M. 68 years old. 8 years	Mr. Symonds's case. Had been operated upon for simple fibrous stricture of pylorus eight years before.
7 Various	158.40	5.00	3.16	12.6	F. 59 years old. 20 days	Mr. Swan's case at Cancer Hospital. Partial gastrectomy for cancer, and posterior gastro-jejunostomy.

Comparison of these tables shows that upon a milk diet (Cases 1 and 2) the absorption of fat was impaired to a slight but definite amount. Cases 4 and 5, on the other hand, which were fed upon a mixed diet rich in fat, digested larger quantities of fat with complete success. This result is, perhaps, interesting, because it gives support to the practice of surgeons who usually advise the abandonment of a purely milk diet as soon as possible after gastro-jejunostomy. Again, an examination of Tables III. and IV. tends to show that the result is the same whether there is or is not pyloric obstruction, whether the duodenum is or is not excluded from the intestinal tract. Cases 1 and 4 had pyloric obstruction, Cases 2 and 5 had no pyloric obstruction at all. It follows that the explanation of the deficient absorption of fat in Table III. is not to be found in the short-circuiting of the duodenum, and in the consequent want of contact between acid chyme and duodenal mucous membrane. The cause must be common to both obstructed and non-obstructed cases, and it is later suggested that it is to be found in the regurgitation of alkaline duodenal juices through the artificial opening, with the consequent diminution of the acidity of the stomach contents, both by chemical reaction and reflexly by inhibiting the secretion of acid gastric juice.

The evidence for this regurgitation through the artificial opening rests partly upon the work of Katzenstein.<sup>5</sup> In dogs, with gastro-enterostomy performed, this worker showed that bile and pancreatic juice always found their way into the stomach, at first continuously, later after the ingestion of food. This regurgitation is hastened by the presence of fat in the food. In consequence the stomach acidity is reduced both by chemical reaction and also by reflex inhibition. That the introduction of alkalis into the stomach reflexly inhibits the flow of acid gastric juice—a fact first shown by Pawlow experimentally—is further proved by the observation that after gastro-enterostomy the total chlorides in the stomach are diminished.

Clinical evidence also bears out the findings of Katzenstein. In a patient upon whom gastro-jejunostomy had been performed four months previously, Katzenstein himself showed the presence

of bile and pancreatic juice in the stomach after an ordinary test meal. Kaiser<sup>6</sup> quotes numerous observers who found that after gastro-jejunostomy in human beings bile was almost invariably present. A case under the care of Dr. Hale White, upon whom gastro-enterostomy had been performed more than a year previously, and who suffered from persistent vomiting, consistently showed absence of free hydrochloric acid and the presence of bile in the stomach. In this case Mr. Laidlaw found in the washings of the stomach a trace of an alcohol, which was taken to be evidence of the existence of alcoholic fermentation of the carbohydrates of the food, and Dr. Eyre subsequently cultivated a yeast from the stomach contents submitted to him. Upon a diabetic diet, and with the addition of a considerable amount of weak hydrochloric acid, the patient made considerable improvement. This case is perhaps interesting, because it suggests that persons with gastro-enterostomy may run a certain risk from the removal of the antiseptic power of the gastric juice. A yeast is by no means the most virulent organism with which the human stomach may be called upon to deal.

In this regurgitation of alkaline bile and duodenal contents there may be found the explanation of the figures in Tables III. and IV. Whether or not there was obstruction at the pylorus, the results were the same. Upon a milk diet in both cases an equal impairment was found; upon a mixed diet rich in fat, in both cases the absorption of fat was within normal limits. The explanation of the impairment in fat absorption in cases on a milk diet must be found in some abnormality common to both obstructed and non-obstructed cases. In the former all the stomach contents leave by the artificial opening; in the latter little or no escape takes place through it. In both the stoma remains patent and permits regurgitation.

That the impairment of fat absorption is confined to cases upon a milk diet further requires explanation. That it is not simply due to the unappetising character of a milk diet, and consequent diminution of the psychic flow of gastric juice, is proved by a comparison with Table I., where the results of experiments upon a milk diet equally unappetising

are given. Moreover, in Cases 1 and 2, the digestion of proteids was complete. It is possible that with the diminution or disappearance of the stomach acidity the rennin acts at a disadvantage. The effect of the presence of rennin in the stomach under normal conditions is to cause coagulation of the cow's milk into a dense clot. In this way the too rapid escape of the milk is prevented. With the appearance of the alkaline bile in the stomach it is possible that the formation of this dense clot is prevented, and that the explanation lies in the abnormal rapidity with which the milk escapes. That this is a possible explanation is further suggested by Case 3. Here no gastro-enterostomy properly so called was performed, but the pylorus, and the pylorus only, was excised, and an end-to-end anastomosis made. The patient, who suffered from a simple fibrous stricture of the pylorus, after the operation passed 26·28 per cent. of the fat of her milk diet undigested. The result of such an operation must have been to remove the carefully adjusted regulating mechanism of the pylorus. Serdjukow has shown that the pylorus opens and shuts in obedience to an elaborate local nervous reflex, the stimulus being provided by the presence of free acid on the gastric side of the valve. Referring to this action of the sphincter, Pawlow remarks: "This regulating action prevents disorder in the process of digestion and at the same time ensures regularity in the transition from the acid gastric to the alkaline intestinal digestion." With the pyloric valve removed the gastric contents escape with undue rapidity, while regurgitation of alkaline duodenal contents is no longer prevented. The large amount of undigested fat found in the fæces in Case 3 may be explained if we consider how rapidly the milk, prevented from undergoing complete coagulation by the regurgitation of bile and alkaline duodenal juices, would escape from a stomach which had been deprived of its pyloric sphincter. That the amount of undigested fat was larger than in Cases 1 and 2 may further be explained when we consider that in Case 3 the abnormal opening was in the direct line of the forward peristalsis of the stomach.

The results of Tables III. and IV., therefore, lend some support to the belief that alkaline bile and duodenal juices constantly regurgitate through the stoma. Moreover, while it is true that peptic jejunal ulceration is from time to time recorded after gastro-enterostomy, the extreme rarity of these cases is in itself evidence that the gastric acidity is diminished. For if the acidity were normal we should expect such ulceration to be comparatively common, as a result of the uncontrolled escape of the gastric contents through the artificial opening, and of the insufficient neutralisation which would result.

The practical importance is, that in this regurgitation of alkaline duodenal contents lies the explanation of the utility of gastro-enterostomy in cases of peptic ulcer. Peptic ulceration of the alimentary tract, as is well known, is confined to those regions where the reaction is at times acid, viz., the stomach, the first part of the duodenum, and, with extreme rarity, as a sequel of gastro-enterostomy, the jejunum just below the artificial opening. If the reaction of the stomach could be made entirely and permanently alkaline, the cure of gastric ulcer would be facilitated, and relapse rendered in the highest degree unlikely. If, after the performance of a gastro-enterostomy, the proximal loop were divided close to the stoma, and the ends closed, the bile and pancreatic juice would be forced to pass backwards through the pylorus in the reverse direction to reach the stomach. Such an operation would deprive the stomach and the upper part of the duodenum of their individual acid reaction, and reduce them for good and all to the alkaline level of the rest of the alimentary tract. This operation has, indeed, been undertaken more than once. Moynihan<sup>7</sup> has reported a case where he was forced to adopt this procedure because of the accidental rupture of the duodeno-jejunal flexure. The patient made a good recovery, without vomiting or wasting. Tavel, of Berne, has reported a similar case, quoted by Moynihan,<sup>8</sup> where persistent vomiting after gastro-jejunostomy, unrelieved by several secondary operations and anastomoses, was finally cured by adopting this method.

Recently Maury<sup>9</sup> has more than once performed the operation upon dogs, and the animals have lived and suffered but little inconvenience. Fortunately such severe measures are not usually called for. In the majority of cases a simple gastro-enterostomy will bring relief or effect a cure. The testimony of surgeons upon this point is almost unanimous. It would appear, however, from the foregoing considerations, that a distinction should be enforced between gastro-enterostomy done for drainage in pyloric obstruction and the same operation done for ulceration of stomach or duodenum without obstruction. In the former the object is to secure a maximum of drainage with a minimum of regurgitation, while in the latter the operation should encourage a due amount of regurgitation. Surgeons, it is true, have not as yet advocated any difference of procedure in the two cases. It is certain that in the first group, where the object is to provide drainage, the opening will best fulfil its function when it is situated as near the pylorus as possible. It will then be as nearly as possible in the direct line of forward peristalsis, and will most nearly approach the normal arrangement of parts. If the opening is placed further from the pyloric end, the drainage is thereby rendered less effective and the vomiting is apt to continue unrelieved. The question then presents itself—would vomiting also continue if the opening was placed away from the pylorus, in cases where there had been no obstruction? Such an arrangement would certainly tend to encourage a due amount of regurgitation.

The statistics of gastro-enterostomies have not yet been separated into these two groups, and, until this is done, it is possible to maintain that the ill-results of placing the opening elsewhere than at the pylorus would only be apparent in cases where there is obstruction. That the mere presence of bile in the stomach is in itself a quite insufficient explanation of prolonged vomiting after gastro-enterostomy, is proved by the absence of vomiting in the cases of Moynihan and Tavel quoted above, as well as by the observations of Kaiser, Katzenstein, and others. Equally striking is the statement of Cannon and Blake,<sup>10</sup> that in their researches upon cats upon which gastro-jejunosomy had



been performed, repeated vomiting after the operation, such as attends the so-called "vicious circle," was usually associated with kinks, and demonstrable obstacles to the easy passage of the food.

It is possible that, in gastro-enterostomy performed for ulceration without obstruction, it would be of benefit to make the opening at some little distance from the pylorus, where the pressure within the stomach is relatively low. In this way the regurgitation of alkaline duodenal juices would be encouraged. However this may be, it is certain that in all such cases a simple gastro-enterostomy by the no-loop method should be performed, and that the Y-shaped junction and secondary entero-enterostomies—all of which militate against this regurgitation—should be avoided. From this point of view, it is interesting to note that, since January, 1905, guided entirely by observation of the results obtained, the brothers Mayo have entirely given up the more complicated methods, and always perform the simple no-loop operation.

Case 6 was examined because it provided an opportunity of investigating the power of absorption of fat in a patient upon whom gastro-enterostomy had been performed for simple fibrous stricture of the pylorus eight years before.

Case 7 was the only case of malignant disease examined. In both, the digestion of fat, upon a mixed diet rich in fat, was normal.

Finally, I have to thank the physicians and surgeons under whose care the patients were at Guy's Hospital, and Mr. Swan, at the Cancer Hospital, for their kindness in so readily granting facilities for the work.

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# MYASTHENIA GRAVIS.

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By

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Thesis for the Degree of M.B. Cambridge.

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IN the year 1906, two cases of this rare and interesting disease, one having a fatal issue, were treated in Guy's hospital. The following accounts are based on Ward and Pathological Reports, supplemented by personal observations:—

CASE 1.—John S., æt. 60, retired soldier, admitted February 14th, 1906, under Dr. Taylor, in Addison 49, for inability to bring the jaws together and ptosis of right upper eyelid. He had served many years in China. Has never had any serious illness or venereal disease. The present trouble started five weeks ago with pain in the right side of the neck and weakness of the muscles of the back of the neck, so that the head when bowed forward could only with much exertion be held upright. In order to see to walk he supported his head with his hands. Two weeks later drooping of right upper eyelid appeared, interfering with vision, and very soon inability to properly masticate food, because he could not bring his jaws together. During the last few weeks he has felt himself growing weaker and less able to undergo muscular exertion. He has fed on slops.

*Condition on admission.*—Pulse 72, temperature 96°, respiration 24. Patient is of spare build and good muscular development. He looks fully his age. There is marked ptosis of right eyelid and a dropping of the lower jaw. The head can be held erect for a time and then drops forward, but after it has been supported

by the hands for a short time can again be held up. Speech very indistinct, slurring and mumbling, rectified by supporting the lower jaw, when it becomes fairly distinct.

*Details.*—Right eyelid is not paralysed. The lid can be partly raised, but soon droops. The left lid is normal. Orbicularis palpebrarum normal both sides. No ophthalmoplegia, nystagmus or change in fundus. Pupils react well. No sign of facial paralysis. Can whistle and project tongue fully in the mid line. Can close jaws fully for a moment, during which the masseters feel firmly contracted. Cannot masticate solids, but can swallow fluids and soft food quite well. Can close lips tight, the buccinator and other muscles acting quite well. The falling of head is due to weakness of the muscles at the back of the neck, *i.e.*, upper fibres of trapezius, splenius capitis, etc. No visible muscular atrophy. Muscles of abdomen and extremities apparently normal. Knee-jerks brisk. No ankle clonus. Plantar reflex flexor. Sensation good throughout. Special senses, sight, hearing, taste, unimpaired. No evidence of syphilis.

*Circulatory system.*—Pulse 72, moderate tension, regular. Artery thick and tortuous. Heart apparently normal.

*Respiration.*—Lack of free movement of whole chest during respiration. Abnormal length and loudness of expiration on auscultation.

*Alimentary system.*—Teeth bad, many loose. Tongue slightly furred, moist. Appetite good. Bowels irregular.

*Urine.*—Specific gravity 1000·2, straw colour, neutral. No abnormal constituent.

February 15th. Dr. Taylor put the patient through the alphabet. He could pronounce each letter distinctly and quickly while he held the jaw up with his hand, but on removing it was unable to do so. Pronunciation of P and X especially bad. Though he had some weakness of the legs he walked up and down well.

16th. Remained out of bed all day. After some time there was general muscular weakness, especially in the mid-dorsal, lumbar and cervical regions. Diet consists of soft foods, as he could not chew meat.

20th. Still up. No change.

23rd. Some ptosis now in the left eyelid and that on the right side more marked. He soon tires with walking, becoming bent as if the spine had given way, while the knees seem to give under him. After a short rest he soon regains strength. Very low spirits.

27th. Because of increasing weakness he is now confined to bed. Ptosis of left lid very marked. He complains of a suffocative feeling, as it were of a tight band fixed round his chest. This comes on in attacks, which do not cause obvious distress.

#### ELECTRICAL REACTIONS.

*Qualitative changes.*—On the trapezius anode closing contraction is greater than kathode closing contraction, an abnormality present only in this muscle.

*Quantitative.*—Biceps to galvanic current: 100 consecutive stimuli. Last contraction quite as good as the first. Subjected to 100 consecutive faradic stimuli, contractions weakened after the 60th.

Trapezius.—Galvanic; 100 consecutive stimuli. No weakening.

*Faradic.*—100 consecutive stimuli, weakening after 60.

Masseters.—Galvanic; 100 consecutive stimuli. Last contraction strong as first.

*Faradic.*—Contractions much weakened after 90th stimulus.

*Comment.*—We may therefore conclude that myasthenic reaction was present, and slight reaction of degeneration present only in the trapezius.

March 1st. Depression great. Attacks more frequent and longer. During them the patient's appearance is normal, and there are no abnormal physical signs in the chest.

2nd. No appetite. Slight difficulty in swallowing. This morning he expressed fear of impending death in these suffocative attacks. Pulse, which has previously ranged from 80—90, has risen to 100. Same day, death at 12.20 p.m. At twelve o'clock

he took some milk and did not appear to have changed. Shortly after he drew his bed curtains together. When they were pulled back a few minutes later he was found dead.

*Autopsy.*—Performed next day by Dr. Fawcett. Pleura: old adhesions, right base. Lungs: rather emphysematous. Kidneys: congested. Testes: normal. No scars on penis or body. Brain: no meningitis present; no naked-eye signs of change in the brain substance.

The following specimens were reserved for microscopical examination:—

Pons and medulla.

Right and left levator palpebræ superioris muscles.

" " masseter muscles.

Trapezius muscle.

Dr. E. Farquhar Buzzard very kindly examined them, and wrote to me as follows:—"The parts of the central nervous system were normal. The peripheral nerves showed no change. In the left masseter, and the right levator palpebræ superioris, were fairly numerous 'lymphorrhages,' such as I have described in other cases."

CASE 2.—Mary G., æt. 24, mill hand in silk factory, admitted February 7th, 1906, under Dr. Hale White, into Mary Ward, for weakness of arms and inability to swallow.

*Family history.*—Father died at sixty-three, mother at fifty-six of consumption. She has two brothers, one of whom is "declining."

*Previous illnesses.*—Scarlet fever as a child, pleurisy two years ago.

*Present illness.*—Began five months ago, in September, 1905, with difficulty in swallowing. Fluid returned through the nose. Speech was affected, articulation often being quite impossible. Shoulder muscles began to get weak, and she complained of being unable to do her hair. Both upper extremities became weak, and things would fall out of her hands. For the last few months her sight has been hazy. Incontinence of urine. Constipation obstinate, occasionally lasting from fourteen to fifteen days. For some time there was complete loss of control of

tongue movements. January of this year she spent in Halstead Infirmary, being fed through the nose. The fortnight before admission she brought up, in the morning, a quantity of phlegm, occasionally blood-streaked. She has no cough. During the illness there has been great loss of weight.

*Condition on admission.*—Temperature 97°, pulse 65, respiration 20. She has dark hair, pale face, black eyes, and is about five feet high. Teeth defective. Liver and spleen not palpable.

*Respiratory system.*—Chest normal in movement, voice and breath sounds, etc.

*Heart.*—Impulse in fifth space  $\frac{1}{2}$ -in. internal to nipple line. Sounds normal.

*Pharynx.*—Of two portions of water the first was swallowed after thirty seconds struggling, the second caused so severe a choking sensation that it could not be swallowed at all.

*Nervous system.*—General weakness, becoming much greater after exertion or emotion; less during rest. Says she is much worse during cold weather. Unaffected by menstruation.

*Arms.*—Biceps, triceps, pectoralis major, and deltoid act well, though the movements are somewhat inco-ordinate. Hand grip very weak. Paresis of interossei; she is unable to separate the fingers to normal extent, and unable to bring them together. Unable to appose thumb and little finger. Main en griffe. Ulnar reflex slightly marked. Sensations of pain, heat, cold and touch greatly impaired. She cannot distinguish touch by two points at considerable distance apart, e.g., 2 cm. on forehead. Muscular sense good. She can tell the heavier of two weights. Knees weak, one finger being sufficient to prevent their being raised. No wasting. Extremities of both sides equally affected. Knee-jerk normal. Plantar reflex flexor. No ankle clonus.

*Face.*—Bilateral ptosis. Weakness of orbiculares palpebrarum. No other paresis of facial muscles. She can whistle or show teeth.

*Special senses.*—Great variations in relative positions of eyeballs. When she first looks at an object, the visual axes are parallel; this is replaced by a gradually increasing convergent

squint, which is well marked after two minutes, the left external rectus being especially weak. Reaction to light and accommodation good. Vision misty, especially in right eye. Diplopia when she looks to the right. By the ophthalmoscope the vessels are seen to be straight. Edge of the disc not well defined, and the whole disc has a speckled appearance.

*Voice*.—When she starts conversing the voice is almost natural, but after a few moments it takes on a nasal twang, and then becomes less and less distinct, the words becoming slurred. After a few minutes it is unintelligible. There is a sense of fatigue.

*Laryngeal cords* are seen to move well.

*Taste* is said by patient to be not so good as formerly, and is better on the right side of the tongue.

*Smell* normal.

*Tongue* cannot be fully protruded. Movements otherwise normal.

#### ELECTRICAL REACTIONS.

*Faradism*.—Thenar muscles, interossei and right deltoid, gave diminished contractions.

*Galvanism*.—(Current of  $\frac{1}{10}$  m. amp.) Thenar and hypnothenar muscles, diminished contraction; right and left trapezius, left triceps and left median nerve, increased contraction.

*Qualitative*.—Hypothenar — ACC < KCC.

Interossei (4th space) ACC < KCC.

No myasthenic reaction (Mya. R.). The extensors of the right forearm stimulated 80 times by faradism gave no deterioration of contraction. Thenar muscles stimulated 50 times gave like result. Some muscles reacted similarly after 100 galvanic stimuli.

*Urine*.—Specific gravity 1000. Urea 1 per cent. No albumen or sugar.

February 8th. Condition unaltered. She is on nasal feeds.

17th. Orbiculares palpebrarum much stronger. Strabismus hardly noticeable.

21st. Owing to regurgitation of the nasal feeds patient has been fed by nutrient enemata since the 18th until to-day. She has to be propped up, as she has a choking sensation when she lies down flat. Phlegm collects in the throat. Speech very weak.

28th. Patient getting stronger. Speech practically normal. No paresis of left external rectus, the eyes moving normally in any direction. She can do needlework, and takes bread and butter well.

March 8th. Improvement continued until to-day, when speech became worse. There is now no strabismus nor ptosis. Arms are stronger. She can lift fairly heavy articles and approximate thumb and little finger.

12th. Slight paresis of left external rectus has recurred. Speech now reduced to a nasal whisper. There is much difficulty in swallowing fluids.

April 4th. Fainting attack to-day. There has been no incontinence since admission.

May 5th. She takes solids more easily than fluids. General condition better. She reads a book well, but has to keep her right eye shut, otherwise she finds the words run together.

9th. Pain in right arm. She can raise the arm six times against resistance without fatigue, but after that requires greater efforts each time, till finally she is unable to move it.

17th. Slight choking attack accompanied by gurgling in the throat. An emetic being inefficacious, the stomach tube was used, which produced relief.

19th. Attacks of choking and coughing have recurred several times, during which her condition becomes rather serious.

21st. She is now much better and is free from respiratory disturbance.

June 7th. She was sent to-day to Halstead, Essex, where she was admitted into the infirmary.

Dr. H. Ashworth has kindly written to me about her on two occasions, as follows :—

15th September, 1906. "I am glad to say she seems a little better ; has had but one choking attack since admission, and is



able to take food without requiring nasal feeding. She gets up daily."

2nd February, 1908. "I believe Emma G. is improving. She has not had to be artificially fed for some months. There is no strabismus, and the vision does not get worse. The difficulty about the latter is the ptosis, as when she raises the lid with her hand she can see better. At times her speech gets worse and then improves again."

It has been my task to collect the literature on the subject of *Myasthenia Gravis*, which has appeared *since* the publication by Campbell and Bramwell of sixty cases in *Brain*, 1900. In addition to the two Guy's cases which I was fortunate enough to watch, I have been able to collect 124 others, the abstracts of which are appended later. I have to thank Dr. Frederick Taylor and Dr. Hale White for kind suggestions and for permission to publish their two cases, and also Prof. Sir Clifford Allbutt for valuable criticism. I have also been much aided by Dr. E. F. Buzzard's work.

*History.*—This disease should present special interest to all Guy's men, as it was first described by Sir Samuel Wilks, in the *Guy's Hospital Reports* of 1877, where he records a case of apparent bulbar paralysis without discoverable lesion in the medulla. This may be regarded as the first account possessing any claim to precision, though Dr. Guthrie<sup>50</sup> has drawn notice to a suggestive passage in a book, published in 1685, entitled, "The London Practice of Physick, or the whole Practical Part of Physick contained in the works of Dr. Willis." When describing "The Palsey," he tells of a special variety of sufferers—"Those who, being troubled with a scarcity of Spirits, will force them as much as they may to local motions, are able at first rising in the morning to walk, move their arms this way or that, or to lift up a weight with strength, but before noon the stores of the Spirits which influenced the muscles being almost spent, they are scarce able to move hand or foot. I have now a prudent and honest woman in cure, who for many years has been obnoxious to this kind of bastard Palsey, not only in her limbs, but likewise in her

tongue. This person for some time speaks freely and readily enough, but after long, hasty, or laborious speaking, presently she becomes mute as a fish, and cannot bring forth a word, nay, and does not recover the use of her voice till after an hour or two."

The first differentiation of the disease as a clinical entity was made by Erb, in 1879, in a paper entitled, "Clinical Observations of Bulbar Paralysis." Under the subheading, "On a new, probably Bulbar group of symptoms," he describes three cases, characterised by ptosis, weakness of the neck, jaw muscles, and extremities, disturbances of speech and deglutition. In the absence of an autopsy, he believed the symptoms to be due to some lesion in the upper part of the medulla.

In 1886 and 1887, cases were published by Jendrassik, Oppenheim and Eisenlohr, under varying titles, "Bulbar Paralysis without Anatomical Lesion," "Asthenic Bulbar Palsy," etc. The next contribution to the study of the disease was made in 1891, by Goldflam, who showed that the muscles were not absolutely paralysed, but tired with abnormal rapidity. In 1895, Jolly called attention to the presence of a peculiar "myasthenic" reaction to electrical stimuli. Five years later appeared Oppenheim's<sup>8</sup> monograph, and the series of sixty cases published by Campbell and Bramwell, in *Brain*, 1900, the last series of any magnitude that we can find published.

In 1901, the first pathological finding of note was made by Weigert,<sup>15</sup> who, in a typical case of myasthenia gravis, found a sarcoma of the thymus and secondary infiltration of the muscles by foci of lymphoid cells. Similar foci, termed "Zellherden," or "lymphorrhages," were later found by R. Link<sup>49</sup> associated with a persistent thymus and, independently of abnormalities of the thymus, by Buzzard<sup>48</sup> in this country.

#### ETIOLOGY.

*Sex.*—Of the 114 cases tabulated by Hun, 72 were females, who thus stood in proportion to males as 1:2. Oppenheim reckoned the proportion as 3:2. Of my own 126 cases, 76 were females, 50 males.

*Age.*—According to Goldflam,<sup>80</sup> chiefly 22–30 years. Of our cases the ages run thus:—

Males.	20–30 years	...	...	...	15 cases.
	30–40 "	...	..	...	15 "
	Under 20 "	...	...	...	5 "

(The youngest are 4½—Goldflam. 15—Grund.<sup>121</sup> 2—Sterling.<sup>71</sup> 5—Von Michel.<sup>63</sup> 11—Guthrie.<sup>124</sup>)

Over 40 years	...	...	...	15 cases.
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(71—Hingston and Stoddart.<sup>85</sup> 62—Fajersztaju.<sup>89</sup> 61—Goldflam.)

Females.	20–30 years	...	...	...	36 cases.
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Under 20 "	...	...	...	9 "
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(14 years—Gowers.<sup>31</sup> 15—Wassing.<sup>80</sup>)

Over 40 years	...	...	...	8 cases.
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(*e.g.*, 63 years—Michell Clarke.<sup>87</sup>)

From which we conclude that the cases are most commonly affected between twenty and thirty in women, and in men at older ages.

*Race.*—Myasthenia appears to have a very wide geographical distribution, America, Australia and most European races having contributed to our series of cases, which includes 1 Negro and 4 Jews; 28 cases (one a Russian Pole) are contributed by British observers. One case is reported from Japan (Noogazawa, Tokio—Izi-Shinohi, 1905, 185–190).

*Occupation.*—In a fair number of cases occupation has been such as to demand close application to work indoors, schoolmasters, clerks, milliners, mill hands, *e.g.*, Emma G. Often for long hours. Leclerc and Savonat<sup>86</sup> declare that seamstresses and tailors furnish more than a quarter of the cases, a statement not borne out by our figures, which also show that country labourers and children from mountain districts are not immune.

*Predisposing causes.*—Definite predisposing causes are mentioned in 55 of my cases. They may be divided into the following groups:—

*a.* Emotion, shock, worry, recorded in 11 cases. Thus Auerbach<sup>82</sup> describes the onset in a woman of twenty immediately after a shock, Launois<sup>80</sup> narrates a case following depression after a bereavement. Business worry (Hogg<sup>80</sup>), fright (Muskens<sup>98</sup>).

*b.* Overwork, mental or physical, and lack of sleep (11 cases) Thus overwork and long hours (Pel<sup>69</sup>), overwork in a servant (Hödlmoser<sup>24</sup>), fatigue of nursing (Hey<sup>51</sup>). This cause is frequently combined with the previous group, *e.g.*, overwork and grief in a seamstress (Goldflam, case 5), overwork and emotion (Trömner<sup>106</sup>).

*c.* Some infective fever or chill.

*Influenza*—Five cases come in our series (Dodd,<sup>75</sup> Sossedorf,<sup>cit. 8</sup> Hirschl,<sup>105</sup> etc.).

"*Chill.*"—Four cases (Guido Bini.<sup>98</sup> Oppenheim).

*Recurrent tonsillitis.*—Two.

*Syphilis*, or para-syphilitic affections, *e.g.*, tabes (Charpentier<sup>64</sup>) three cases.

*Rheumatic fever* (Ventra<sup>12</sup>).

Some *intoxication*, especially those connected with disordered glandular functions.

An interesting connection may be traced between myasthenia and disordered functions of the thyroid gland. Seven of our cases are associated with Graves' (or Basedow's) disease, *e.g.*, Löser<sup>108</sup> records two cases.

1. Girl, æt. 21, showing an intermittent ptosis of a myasthenic character, with tremors, persistent tachycardia, slight goitre, and exophthalmos.

2. Woman, æt. 35. Long history of goitre, exophthalmos, tremors, later ocular symptoms of myasthenia.

Goldflam, case 2, narrates a case of myasthenia who since childhood had had a goitre and prominent eyeballs. Meyerstein<sup>44</sup> records a similar case in a seamstress. Another, perhaps doubtful case, is given by Brissaud and Bauer.<sup>70</sup> A patient of Muskens<sup>96</sup> had exophthalmos without goitre. Similar cases have, previously to 1900, been recorded by Oppenheim, Remak, Finizio, Karplus, Murri, Punton.

In this connection we may point out that exophthalmic goitre is generally associated with certain nervous symptoms, and in some cases with paralysis of face, chewing muscles, tongue. Ocular paralyses, *e.g.*, third nerve (Finlayson, Brain, 1890),

trochlear (Möbius Spec. Path. Ther. von Nothnagel, XXII.), and even bulbar symptoms, as trouble in swallowing, nasal speech, paresis of vocal cords (F. Müller, Deutsch. Arch. Journ. Klin. Med., XLI.), Bristowe, Brain (85, P. 313), are recorded in cases which at autopsy present no causative lesion.

Simple goitres are seen in three cases, myxœdema in one, a patient of Chvostek,<sup>128</sup> who informs us that the myasthenia was cured simultaneously with the myxœdema.

Rennie<sup>67</sup> records the case of an Australian jockey, who had taken thyroid to excess for two years, in order to reduce his weight, and developed myasthenia after a fall from his horse.

The use of thyroid extract during the disease appears to have little or no effect.

The relationship to disease of the thymus will be discussed later (*vide* Pathogenesis).

*Pregnancy or lactation* has a distinct connection with seven cases. A most interesting account is given by Warrington<sup>68</sup> and Gemmell<sup>78</sup> of a woman who noticed, during the first months of pregnancy, weakness in her limbs, which rapidly progressed, and was very marked when the child was born. Eighteen months later, again pregnant, she first came under observation with well-marked signs of myasthenia gravis. With advancing pregnancy she became much worse, suffering from exhaustion and attacks of dyspnœa. Her condition was so grave that Cæsarian section was performed, with great success. She was delivered of a healthy child, and steadily improved during the puerperium. Indemans' case<sup>79</sup> had a sudden excess of symptoms during her third pregnancy, while Fabrio, Pietro<sup>117</sup> records a case which appeared to follow frequent pregnancies. Pregnancy in an epileptic is given as an exciting cause by R. Kohn,<sup>46</sup> lactation by Goldflam (case 5), accouchement, in a woman deserted by her husband, by Dupré.<sup>77</sup> A fatal case, dating from abortion, has been described by Burr and McCarthy.<sup>14</sup>

On the other hand, myasthenic women may pass through childbirth without perceptible change in their condition.

## CLINICAL FEATURES.

*Onset.*—Out of our 126 cases, in 56 the onset has been expressly stated to have taken the form of some ocular paralysis or paresis, most frequently ptosis, sometimes diplopia, in consequence of which they may first be seen by the ophthalmic surgeon. In not a few of these, however, there have been preliminary headaches, subjective sensations, or pains of some sort. Thus, in one case of Buzzard's (case 3) headache and vague pains preceded stiffness of the eyelids, while in his second case pains all over and a sensation of pins and needles in the finger tips were followed by double ptosis. Similar premonitory symptoms are recorded by other observers; darting pains (Brissaud<sup>70</sup>), headache (Boldt<sup>110</sup>), pains in limbs (Schüle<sup>1</sup>), general tiredness (Chvostek,<sup>123</sup> S. Brown<sup>5</sup>).

The ocular symptoms may be of sudden occurrence, *e.g.*, sudden diplopia (Oppenheim<sup>8</sup>), and may precede the general symptoms by a long interval. Thus, in a case of Goldflam, temporary bilateral ptosis occurred seven years before any further development.

In the absence of ocular symptoms, we find most frequently some other bulbar symptom, *e.g.*, difficulty in speech, sometimes sudden (Muskens,<sup>86</sup> case 1), difficulty in swallowing or in moving lips, or nasal voice.

A fair number commence with weakness of the extremities. They are noticed to drop things frequently (Leclerc<sup>86</sup>), or have frequent falls (Grund<sup>121</sup>), the knees giving way.

*Motor symptoms.*—The cardinal feature of the disease is rapid muscular fatigue associated with paresis of varying constancy, which may become a definite paralysis. It is spread, in the majority of cases, over the greater part of the body, but is most marked in certain special muscle groups, particularly in those which derive their nerve supply from the bulb. It is generally bilateral, though it may be greater on one side.

*Ocular muscles.*—In all but sixteen of our cases some ocular paresis is mentioned.

Ptosis was found by Riggs<sup>103</sup> to occur in 75 per cent. of cases, and occurs in still greater proportion in our list—110 out of 123.

It is generally first unilateral, later bilateral, and very variable in degree, disappearing sometimes, but seldom permanently. Before its onset the patient may complain of a stiff or tired feeling of the eyelids.

The orbiculares palpebrarum are frequently weak, causing different degrees of lagophthalmos. External ophthalmoplegia is nearly as frequent as ptosis.

It is pointed out by Gowers<sup>31</sup> that the ophthalmoplegia resembles that of nuclear degeneration, with the following noteworthy differences:—1. The partial escape of the muscles which move the eye downward. 2. The constant and irregular affection of the lateral muscles differing in degree in associated muscles and varying much at different times. If definite strabismus, either convergent or divergent, be not noted, there is some relative muscular insufficiency, causing either eso- exo- or hyperphoria (Wescott<sup>47</sup>) with diplopia as the natural sequela. This, like the general symptoms, is worse, or may only appear in the evening. Paralysis of convergence may occur (Wescott,<sup>47</sup> Gowers<sup>31</sup>), and that, too, as in Gower's fourth case, though the internal recti may act well for lateral movements.

There is a definite class of cases where ocular symptoms predominate. Thus Spiller<sup>74</sup> records a definite case of myasthenia confined to the eye only, presenting varying ptosis, diplopia, and apparently astigmatism ("things looked crooked").

Another case (Frank<sup>76</sup>) began with ptosis, followed by convergent strabismus and defective movement of all external eye muscles, except left external rectus. There were no general paralyses. Similar cases are recorded by Wescott<sup>47</sup> and Sterling<sup>71</sup> (case 3). In the latter the main symptoms were ocular, though there was also exhaustion of the abductors of the right arm, and the myasthenic reaction was obtained from the left deltoid.

Associated with weakness of the muscles we find occasional *nystagmus*, or rather nystagmoid movements; in a few constant, in the majority only after forced or repeated excursions of the eyeball. It may be vertical (Hüdlmoser<sup>34</sup>) or lateral, and may occur after repeated lateral movements or after fixed gazing

(Kohn<sup>46</sup>). In lesser degrees the movements are described as ataxic or tremulous.

Affection of the pupillary muscles, as of the sphincters of the bladder and rectum, is rare, though found in some degree in fourteen of our cases.

De Léon<sup>68</sup> records a case in which the reaction to light was exhaustible, and Kollarits<sup>25</sup> a case where it became less with fatigue, but did not disappear.

Hippus (*i.e.*, oscillation of the pupil) occurs in three of our cases—Buzzard,<sup>82</sup> Mendel,<sup>9</sup> Ris. Russell<sup>10</sup> (in the last-mentioned case after long exposure to bright light). Varying inequality of the pupils, perhaps due to tiring of the sphincter, is mentioned by Boldt,<sup>110</sup> Mendel,<sup>9</sup> Sossedorf.<sup>cit. 8</sup> Definite affection of accommodation occurs seldom, if ever, though in one instance (Long and Wiki<sup>17</sup>) the pupils are stated to be very inactive.

The exophthalmos occurring with the joint existence of Graves' disease has been already mentioned.

The facial muscles are frequently involved, resulting in a mask-like, expressionless appearance. The affection is generally bilateral, though unequal on the two sides, while unilateral cases are reported (Burr and McCarthy,<sup>14</sup> case 2). In Gowers'<sup>31</sup> fourth case there is marked difference between the two sides associated with hemiatrophy.

To counteract the ptosis so frequently present we see overaction of the frontalis and excessive wrinkling of the forehead.

This muscle, however, is often weak, which necessitates a backward carriage of the head, as in Gowers' fourth case. Frowning also becomes impossible. The zygomatici and risorius muscles are frequently paretic, causing in the act of smiling an absence of normal movement at the corner of the mouth, while the furrow of the smile is entirely above the upper lip. Attention was drawn by Gowers to this so-called "nasal" smile. The lips also are weak, often producing difficulty in whistling, and, in advanced cases, they cannot be closed for long at a time, so that the saliva is allowed to drop over the chin, *e.g.*, Bramwell.<sup>13</sup> On the whole, the distribution of weakness in the facial muscles resembles that met with in idiopathic muscular atrophy.



The muscles of the jaw fail in many cases. Mastication, normal at the beginning of a meal, very soon tires, or the jaw may drop, as in our own male case, and require support from the hand if the patient wishes to speak.

The soft palate is very frequently affected with resulting nasal regurgitation of fluids, especially at the end of meals, more particularly in the evening.

If the patient attempts to blow out his cheeks, the air escapes through his nose, a somewhat farcical illustration of which is given by Down.<sup>28</sup> A patient who played the "harmonica," suffered, after the onset of myasthenia, from paralysis of the right half of his soft palate, and found that after playing a few minutes he had to desist because the air passed out through his nose, to prevent which he closed his nostrils with thumb and finger, or else with a special spring clip.

These paralyses have an important effect on the speech, alteration of which appears in seventy-seven of our cases. Thus, from paresis of the lip or jaw muscles we get a dysarthria, thickness of speech, or difficulty of articulation. Dejerine and Thomas,<sup>10</sup> Down,<sup>28</sup> Peterson.<sup>40</sup>

If the paresis of the soft palate be at all considerable, as it is in numerous cases, the voice takes a nasal tone. Thus, Bramwell's Scottish case started with a difficulty in speech, which later became nasal. All these effects become much more marked after the patient has been speaking some time.

In conversing with Dr. Hale White's patient, it was most interesting to watch the sequence. At the start her speech was quite intelligible and ordinary, but after a minute it would become nasal, then less clear, and finally, after a few minutes, quite unintelligible, though after a few minutes' rest it would regain its original clearness.

Affection of the tongue occurs in thirty-seven cases in varying forms, the chief of which is failure of protrusion after repeated attempts. The tongue can sometimes be put out only two or three times.

Thus, in a patient of Dr. Buzzard, after twelve attempts at protrusion, the tip could not pass the teeth, mobility being recovered after a minute's rest. Similarly, our female patient could not fully protrude her tongue. Peterson<sup>40</sup> records slight deviation, Giese and Schultze<sup>7</sup> weakness, Priszner,<sup>21</sup> M. Clarke,<sup>87</sup> Sterling,<sup>71</sup> tremors.

Involvement of the tenth nerve is shown in the striking attacks of dysphagia. It was the first symptom in the case of our female patient, who for a long time was fed through a nasal tube. This difficulty in swallowing not infrequently brings on a fatal choking attack.

Saliva cannot be swallowed, and accumulates in the pharynx, whence it is ejected with difficulty. Difficulty in clearing the throat is common.

Campbell and Bramwell found paralyses of the vocal cords in six cases. In the case of our female patient the cords moved well, and I have been able to find records of few laryngeal paralyses, seven in all. In one case (Giese and Schultze<sup>7</sup>), where there was complete aphonia, the cord movements were feeble, especially in abduction. In another (Hödlmoser), the vocal cords were sluggish and the glottis closed incompletely, cf., Raymond and Lejonne,<sup>92</sup> Dejerine and Thomas,<sup>10</sup> Hogg,<sup>30</sup> Gowers,<sup>31</sup> Buzzard.<sup>83</sup>

*Neck muscles.*—These are not infrequently weak and readily fatigued. In our male case the head was held erect for a time and then dropped forward owing to weakness of the upper fibres of the trapezius and splenius capitis, etc. After supporting his head for a short time with his hands he could again hold it up. In the first case of Raymond and Lejonne the tendency of the head was to fall backward, and in the second case it was the anterior and lateral muscles that were weak.

*Trunk.*—The muscles of the back may share in the disorder which produces lordosis or scoliosis (Wassing<sup>80</sup>), or even inability to turn in bed. The abdominal and pelvic muscles may be so weak that the patient requires the help of his hands to raise himself from the recumbent to the sitting posture.

The respiratory muscles are involved in severe cases, in which we find severe attacks of dyspnoea. There may be a preliminary

feeling of tightness round the chest. If the patient is walking along, he may fall down; if lying in bed, he sits up cyanosed, almost suffocated, making weak efforts at expiration. No abnormal physical sounds are audible in the chest except some moist râles and rhonchi, while there is a cough which is too feeble to remove the collected mucus. Sudden death frequently occurs in these attacks, as in the tragic event recorded by Sir Clifford Allbutt. The diaphragm may be uninvolved, as in Buzzard's fourth case, or weak (*e.g.*, Oppenheim<sup>8</sup>), or useless (Giese and Schultze<sup>7</sup>); while Mendel<sup>9</sup> showed in a servant girl under X-rays that its contractions soon diminished.

*Limbs.*—In the great majority of cases these are affected in varying degrees. G. Grund<sup>121</sup> publishes a case in which the symptoms are confined almost entirely to the extremities and trunk. Raymond and Lejonne assert that the muscles nearest to the trunk are the most affected, thus in the upper extremities the muscles of the shoulder girdle, deltoids, rhomboids, pectorals, latissimus dorsi, serratus anticus; in the lower, the gluteals, ilio-psoas, etc. Thus it is very common to find, from weakness of the deltoids, that the patient cannot raise the arms above the horizontal or do her back hair. In some however the fatigue is most marked in the hands. The patient drops things or has difficulty in writing, the first words of a letter being distinct, the later more and more unintelligible.

Dr. Hale White's case had paresis of interossei, being unable to separate the fingers well, or to appose thumb and little finger. Dr. Taylor's case<sup>66</sup> exhibited a difficulty in fine movements, such as picking up pins, while the arms retained fair strength.

If the lower limbs are affected the knees give under the patients as they walk and let them down. Walking may be only possible for a few steps, or quite impossible. In some cases the gait is waddling (Warrington<sup>62</sup>).

The sphincters of bladder and rectum are rarely, if ever, affected, though slight incontinence of urine occurred in our female case, as in those recorded by Von Rad<sup>120</sup> and Wassing.<sup>89</sup>

*Factors influencing condition.*—These cases are nearly always at their best in the morning, when most actions, speech and

mastication, etc., may be well performed, and decline steadily during the day till evening, when they are at their worst.

Exercise always brings on the symptoms, which subside after a rest. When Dr. Hale White's patient started gazing at an object the visual axes of her eyes were parallel. Very shortly, however, there was a gradually increasing convergent strabismus, which disappeared after the eyes had been closed for a short time. General fatigue usually makes individual symptoms worse, and sometimes the exhaustion of one muscle is shared by neighbouring muscles. Thus ptosis in some cases is increased by repeated lateral movements of the eyeball.

Both emotion and cold (as in Dr. Hale White's case) frequently render the symptoms worse. Michell Clarke's<sup>87</sup> case, when cold, lost power in the hands.

Many females are worse at the menstrual period, while pregnancy has, as we have shown, a very bad effect in a number of cases.

It cannot be proved that those groups of muscles are picked out which are in special use by any particular patient.

No cause can as a rule be found for the intermissions and remissions which are so characteristic of the disease. They may last for weeks or months, and, in a case reported by Goldflam, five years, till a relapse occur. During this time the readiness for fatigue may disappear almost entirely, though we find, with few exceptions, slight ptosis or partial paresis persisting.

*Electrical reactions.*—Exhaustion does not occur only to voluntary action, but also to electrical stimuli. This, known as the myasthenic or "Erschöpfung" reaction, has, as described by Buzzard,<sup>88</sup> the following character: With faradic current the muscle rapidly ceases to be tetanised, the subsequent contractions being intermittent for a time, and then ceasing altogether. Voluntary contraction is then much diminished, but not lost; the galvanic reaction is brisk, as is also direct excitability to percussion. The muscle, tired out by voluntary action, shows diminished faradic excitability, but responds well to galvanism and percussion.

Galvanic shocks rapidly repeated for two minutes produce no diminution in the briskness or size of the response. When a faradic current of moderate strength has been applied till no response is obtained, an increase in strength of the current immediately produces a contraction which is rapidly exhausted.

This myasthenic reaction is found in muscles in all parts of the body, sometimes even in those where fatigue is not very obvious, while it may be absent in muscles which would appear to be most affected. Though significant and helpful for diagnosis, it is not pathognomonic, being absent in some obvious cases of myasthenia, while it has been demonstrated occasionally in other diseases, *e.g.*, exophthalmic goitre, hysterical paralysis, infantile paralysis with cortical lesion (Salmon<sup>100</sup>), traumatic neurasthenia (Monguzzi<sup>101</sup>), tabes, cerebellar tumour, disseminated sclerosis (Flora<sup>38</sup>), progressive muscular atrophy, paralysis agitans (Kollarits<sup>26</sup>), Landry's paralysis (Oppenheim<sup>8</sup>), muscular disease, organic disease of pons (Feinberg *Neur. Centblatt.*, 1900, 3). It was found by Kollarits<sup>26</sup> in two cases of cerebellar sarcoma, one of which showed ptosis, the other marked voluntary fatigue of muscles.

The reaction may disappear in remissions of the disease (Goldflam<sup>30</sup>). Raymond and Sicard<sup>83</sup> record its presence for three weeks only during the height of the disease, disappearing with the recovery of the patient.

A somewhat similar reaction is obtained in Thomsen's disease (Steinert<sup>96</sup>). Any reaction of degeneration is uncommon, though occurring in slight degree in both Guy's cases.

*Reflexes.*—Skin reflexes normal. Jaw jerks present in a few cases. Knee jerk, usually rather brisk (said to be exaggerated in twelve cases, Oppenheim,<sup>8</sup> Auerbach,<sup>32</sup> etc.), is sluggish in some instances (Meyerstein<sup>44</sup>). In fifteen of our cases it became more or less exhausted after being elicited repeatedly. Thus, in Hirschl's<sup>106</sup> case, the knee and Achillis jerk tired, though they did not disappear; cf. Buzzard, case 2,<sup>82</sup> Jacoby,<sup>34</sup> Goldflam.<sup>30</sup>

*Palatal reflex* is frequently very sluggish, and may be quite lost.

*Conjunctival reflex* diminished in two instances (Lawford,<sup>65</sup> Leclerc and Savonat<sup>96</sup>).

*Fibrillary* contractions are rare, though seen in a few cases in the tongue, which often may become tremulous after it has been kept out some time (Ventra,<sup>12</sup> Steinert<sup>52</sup>).

*Local atrophy* is markedly absent in most cases which, until recently, has been regarded as a diagnostic point. Buzzard, however, regards it as not uncommon, especially in the tongue. I find definite wrinkling and atrophy of the tongue recorded by Sossedorf,<sup>cit.</sup><sup>8</sup> M. Clarke,<sup>87</sup> Liefmann,<sup>26</sup> Buzzard.<sup>82</sup> The facial hemiatrophy occurring in a case of Goldflam is thought by him to be independent of the disease. Giese and Schultze<sup>7</sup> speak of beginning atrophy of some facial muscles; Dejerine and Thomas<sup>10</sup> of wasting of the thenar eminences; Priszner<sup>21</sup> of muscles of neck and upper arm, thenar and hypothenar eminences; Barnes<sup>115</sup> of masseters and temporals; Fabrio, Pietro<sup>117</sup> of muscles of neck, shoulder, and arms; Buist<sup>11</sup> of flattening of the deltoids. Oppenheim considered this complication to have no part in the disease, while Laquer considered it followed if death were long enough put off. A case of Fuchs' is interesting in this connection. When described in the Wiener klin. Wochenschrift XVI., 1903, p. 513, the patient definitely had no atrophy. A further account in the same Journal, 1904, XVII., p. 1422, tells of the appearance of wasting of the third and fourth interosseous spaces in both hands.

Under the microscope we often see signs of early muscle degeneration, such as later should lead to atrophy. In most cases however there is a striking absence of gross atrophy.

In Buzzard's case 1 the skin of the fingers became thin and glossy, apparently from atrophic change. General emaciation is naturally considerable in those patients that suffer from prolonged dysphagia.

*Sensory*.—It was stated by Campbell and Bramwell that with the exception of a feeling of fatigue in the muscles after exercise, and of stiffness due to immobility, sensory symptoms are seldom present. More recent experience does not confirm that view.

A very large number of the patients suffer from headache, especially at the onset (Boldt,<sup>110</sup> Von Rad<sup>120</sup> and Weigert<sup>15</sup>).

Riggs<sup>103</sup> points out that many commence with occipital pains, which occurred in two of his own three cases and in seven other cases which he collected. In Kohn's<sup>46</sup> case we find constant pain in the forehead, often shooting to the occiput. The headache may be migrainous (Sossedorf, *cit.* <sup>8</sup> de Leon<sup>88</sup>). With pains in the head often occur pains in the limbs (Buzzard) or body (Laquer and Weigert<sup>15</sup>), which may occur alone (Schüle<sup>1</sup>) or with general neuralgic pains (Hingston<sup>85</sup>).

The pains may be darting (Brissaud<sup>70</sup>) or vague (Buzzard). In Buzzard's third case they occur with sensations of formication or pins and needles in the finger tips.

Other localised disorders of sensation may be mentioned, *e.g.*, a burning sensation along the median nerve (Giese and Schultze<sup>7</sup>), stinging, burning pains in the neck and interscapular region (Goldflam<sup>80</sup>), right-sided hyperæsthesia (Mendel<sup>9</sup>), loss of taste (Steinert<sup>59</sup>), diminished sensation to pain, heat, cold and touch (in Dr. Hale White's case), formication of extremities replaced by relative anæsthesia (Launois<sup>80</sup>). "Lightning" pains occur in Buzzard's first and second cases, accompanied in the first by a widespread, and in the second by a small area of relative analgesia and anæsthesia. The fact that the first was associated with diminished knee-jerks aroused the suspicion of tabes, disproved by the autopsy.

Astereognosis, *i.e.*, failure to recognise objects by touch, is seen in two somewhat doubtful cases (Burr and McCarthy<sup>14</sup> and Launois<sup>80</sup>). Dr. Hale White's case had difficulty in recognising two points on the skin. Launois' case shows numbness of the left arm, also present in hands, leg and back in his first case.

Some insensitiveness of the pharynx is mentioned by M. Clarke, and is not uncommon. Vertigo and dizziness are recorded by Goldflam, case 6,<sup>80</sup> Tilney,<sup>113</sup> Wassing.<sup>89</sup>

*Ocular sensory symptoms.*—Stiffness of the eyelids is a frequent complaint (Sterling, case 2,<sup>71</sup> J. Taylor<sup>66</sup>), while the eyes may feel tired (Sossedorf, *cit.* <sup>8</sup> Kohn<sup>46</sup>), or be the seat of dull pain (Byschowsky<sup>86</sup>), or twinges (Link<sup>49</sup>).

Apart from the common diplopia due to muscular errors, in some cases we apparently find defects of vision due to failure of

visual acuity. Thus one myasthenic could not see to read for a long time (J. Taylor<sup>66</sup>); another (Burr<sup>73</sup>) had vision reduced; another "blurred"; another rapidly exhausted (Bini,<sup>68</sup> c.f., B. Lawford,<sup>66</sup> M. Clarke<sup>87</sup>). Micropsia appeared in Goldflam's sixth case, while Burr's patient presented contraction of the visual field and reversal of the fields for red and blue.

*Mental symptoms.*—Very rare. Some of the female cases are emotional or depressed. Actual melancholia is chronicled by Buzzard.

*Lumbar puncture.*—Performed by Raymond,<sup>73</sup> who in the cerebro-spinal fluid showed scattered lymphocytosis. Other results are, no albumen and a slight lymphocytosis (Launois<sup>60</sup>); normal (Brissaud and Bauer<sup>70</sup>).

*Circulatory system.*—Attacks of palpitation may occur with those of dyspnoea, as noted by Oppenheim.<sup>8</sup> His statement, however, that the myocardium is unaffected is denied by Raymond and Lejonne,<sup>92</sup> who state that the X-rays have shown dilatation of the heart under the influence of fatigue. Rapid fatigue of heart muscle is demonstrated by Steinert<sup>62</sup> and Grocco. Raymond and Lejonne's two patients, as also a case of Steinert, had marked low arterial tension (circ. 14, c.m. Hg). Steinert registered 10—12 cm. Hg., hardly varying with fatigue. One case also had a slow pulse. The rate and tension are generally normal, except during the suffocative attacks, a fairly rapid pulse being not infrequent (Mendel<sup>9</sup>), especially if associated with Graves' disease. One of our cases shows intermittent action of the heart.

*Blood examinations.*—Normal (Mendel,<sup>9</sup> Dorendorff,<sup>22</sup> Meyerstein,<sup>44</sup> Diller,<sup>63</sup> Hun, Boldt, Delile, Buzzard). Raymond and Lejonne,<sup>92</sup> in two cases, found a certain diminution in red corpuscles, 3,300,000 and 4,400,000, and a slight leucopœnia, especially in polymorphonuclear cells, which represented, (1) 36 per cent., (2) 53 per cent. of total. The mononuclears were relatively increased, and while rare in a young condition, they were to be seen in the same field full grown or breaking up. They thence deduced that reparation of leucocytes is lacking.

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*Urine.*—Albuminuria occurs in six of our cases ; glycosuria in one (Hingston and Stoddart<sup>35</sup>) ; polyuria, which is found occasionally with organic bulbar disease, in two cases (Steinert<sup>52</sup> and Oppenheim).

*Morbid anatomy.*—Numerous attempts have been made to disprove the German title, "Paralyse bulbare ohne anatomischem Befund," which expressed the opinion of the original observers. Campbell and Bramwell stated that in the great majority of cases in which an autopsy had been made no lesion had been found. They record seventeen post-mortem examinations, in only six of which was anything abnormal found which could possibly account for the symptoms. Chromatolysis in the nerve cells of third, sixth, seventh, twelfth nuclei, degenerated fibres in third, eleventh, and twelfth nerve roots, and recent hæmorrhages in the medullary nuclei were the findings of most importance.

Since that time we have been able to collect the records of thirty-four autopsies, supplemented by the examination of fragments of muscle excised from seven cases, with results which have been by no means negative, and though extremely variable, promise in some respects to throw fair light on the pathology of the disease.

#### BRIEF ABSTRACT OF PATHOLOGICAL FINDINGS.

(References to Numbers of Bibliography.)

1. Schüle.—Old aortic disease, fatty liver. Small recent hæmorrhages in bulb.
2. Hall.—Nothing microscopical in brain or medulla.
4. Paul.—Result of autopsy, negative.
7. Giese and Schultze.—Skull cap very thick. Nothing abnormal in brain, macroscopically or microscopically.
8. Oppenheim.—Recent small hæmorrhages in brain. Muscles normal.  
Sossedorf.—Broncho-pneumonia. Parenchymatous nephritis. Small renal lipoma. Slight degeneration of hinder part of vago-glossopharyngeal nuclei and roots. Tongue muscles seat of atrophy and fatty degeneration.
10. Déjerine and Thomas.—In left ascending frontal convolution, multiplication of neuroglia cells and lack of nerve cells, which show chromatolysis and degeneration of axons. Diminution in large

medullary fibres in medulla. Fatty degeneration of muscle of larynx and tongue, in some fibres the transverse being replaced by longitudinal striation.

14. Burr and McCarthy.—Healed phthisis left apex. Chronic enlargement of spleen and thickened capsule. Right ovary cystic. Thymus enlarged. Four months foetus in utero. Spinal cord unusually broad in lumbar region, and showing persistent postero-median fissure. *Microscopical*.—In medulla chromatolysis of cells of upper nucleus of nerve 10. Atrophy of some of fibres of same nerve. No change in muscles.
15. Laquer and Weigert.—Broncho-pneumonia. Enlarged thymus, with metastatic deposits of thymus structure in deltoid, diaphragm, heart and pericardium.
17. Long and Wiki.—Degeneration of myelin fibres in dorsal region, thickening of vessel walls and neuroglia in dorsal and lumbar swelling. Patch of sclerosis in left lateral column in cervical swelling. Œdema of lungs.
24. Hödlmoser.—Status lymphaticus. Large thymus. Prominent follicles at base of tongue and in intestine. Broncho-pneumonia.
27. Raymond.—No trace of thymus. Lobar pneumonia. Thyroid healthy. Cerebral convolutions congested. Tiny hæmorrhages in cerebral substance at level of bulb and under the pia. Degenerated muscle fibres in left biceps. Nutmeg liver. Hæmorrhages in a lymph gland taken from coeliac region.
30. Goldflam.—Mediastinal tumour (? Sarcoma of thymus).
39. Fajersztajn.—Terminal hæmorrhages in capillaries of central grey matter. Degeneration in intra-medullary roots of nerves, 3, 6, 12. No thymus.
43. Mohr.—Banti's disease. Great puckering of liver. Very large spleen. No gross or microscopical changes in brain or cord.
49. Link, R.—Persistent normal thymus (in a man of 43). Broncho-pneumonia. "Zellherden" in external eye muscles and deltoids.
54. Myers.—Cellular change in cranial nuclei, 3, 6, 9, with some chromatolysis.
69. Hun, Bloomer and Streeter.—Lympho-sarcoma of thymus with metastatic deposits in muscles.
73. Burr.—Abscess in thymus. Recent hæmorrhages in aqueduct of Sylvius. "Lymphorrhages."
77. Dupré.—Persistent thymus (æt. 32). Slight enlargement of liver.
78. Gemmell.—Sections taken at time of Cæsarian section of uterine muscle and rectus abdominis. Normal.
82. Buzzard (Five cases).—All showed "lymphorrhages" in muscles:—1, very large thymus with proliferation and degeneration; 2 and 3, simple hypertrophies of thymus; 4 and 5, normal thymus. Early muscular degeneration.

85. Taylor, J.—Nothing found abnormal.
86. Leclerc and Savonat.—No thymus. Chromatolysis in nerve cells of bulbar nuclei and "olive." Cell substance partly disintegrated.
95. Steinert.—Sections of muscle show foci of lymphoid and epithelioid cells in extra-muscular connective tissue and fatty degeneration of muscle.
107. Sitsen (Pel's case, *vide* 59).—Fresh hæmorrhages under capsule of liver and invasion of leucocytes. Spleen large. Early parenchymatous nephritis. Large thyroid. Muscles, intervertebral ganglia and pituitary body normal.
109. Marburg. — Fragments of muscle excised from two living cases. Muscular lymphoid infiltration and fatty degeneration.
110. Boldt.—Edema of lungs. Heart muscle flabby. Liver small; cirrhotic. Fresh hæmorrhages near nuclei of cranial nerves, 5, 7, 10, 12. "Cell nests" in diaphragm, quadriceps, etc.
111. Borgherini.—Fragments excised from three cases and prepared by Angelozzi's method, *i.e.*, they were enclosed immediately in muscles of a dog or rabbit, which was then killed. Twenty-four or thirty-six hours later they were removed and treated as usual. "Hyaline" muscular degeneration.
113. Tilney.—Colloid cystic adenoma of pituitary body springing from anterior lobe, and therefore related to the derivatives of the pharyngeal ectoderm as the thymus, thyroid, etc. Some cloudy swelling of fibres of deltoid, pectoralis major, and rectus abdominis.
118. Frugoni.—Congenital anomaly in floor of fourth ventricle. Pneumonia. Inflammatory cell foci in substance of muscles. Proliferation of sarcolemma and fatty degeneration.
124. Guthrie.—(1.) A few changes in cranial nuclei, 10, 12.  
(2.) Central nervous system normal.

SUMMARY OF PATHOLOGICAL FINDINGS.

Nothing pathological found ... ..	6
Miliary cerebral hæmorrhages ... ..	6
Minute cerebral changes (chiefly chromatolysis in cells of cranial nuclei) ... ..	7
Localised sclerosis left lateral column (cervical region) ... ..	1
Congenital abnormalities of spinal cord or bulb	2
Atrophy of nerve fibres (slight) ... ..	1
Abnormalities of liver ... ..	6
Abnormalities of spleen ... ..	3
Adenoma of pituitary body ... ..	1
Enlarged thyroid gland ... ..	1
Parenchymatous nephritis ... ..	2
Pneumonia ... ..	6
Pulmonary œdema ... ..	3
Cystic ovaries ... ..	2
Abnormalities of thymus—	
a. With metastatic deposits in muscles...	7
b. Without metastatic deposits in muscles	3
Lymphorrhages (without abnormality of thymus)	5
Muscular degeneration ... ..	5
Examination of excised fragments of muscles:—	
Lymphorrhages and muscular degeneration...	6
Negative (Gemmell) ... ..	1

These “lymphorrhages” are deposits of lymphocytes, forming clumps of various sizes, the largest measuring about 2 by 15 mm., which lie scattered between the muscle fibres, nerve bundles, and blood vessels. They stain with hæmatoxylin and eosin and the ordinary dyes. These Dr. Buzzard regards as constant features of the disease and independent of changes in the thymus, which are absent in two of his cases. Besides the skeletal muscles, he has found them sometimes in the heart, liver, adrenal and thyroid glands. In one instance they were found round vessels in the

substance of the posterior root ganglia, and in another in the peripancreatic tissue. They are frequently seen in the neighbourhood of the capillary blood vessels, from which they apparently originate. They are "not more numerous, if as numerous, in long-standing cases as in those which run an acute and rapidly fatal course." He cannot yet say whether "the prevalence of lymphorrhages in a muscle bears any relation to the functional activity of that muscle." Having searched for them in numerous other conditions he found somewhat similar deposits in one case only—a case of amyotrophic lateral sclerosis. He also found in his cases of myasthenia signs of early muscle degeneration, and no abnormalities in nerve trunks and end plates.

In Dr. Taylor's case, which is reported above, no abnormalities, macroscopical or microscopical, are found except in the muscles in which Dr. Buzzard finds lymphorrhages. These with the other muscle changes seem to be the most definite and consistent phenomena yet described in the morbid anatomy of the disease, the cerebral changes recorded being variable and quite inadequate to account for the symptoms, while the minute hæmorrhages in the brain substance are probably terminal.

We may suggest that, if previous observers had examined the muscles with sufficient care, they would have agreed with the statements of Dr. Buzzard.

As immediate causes of death, pneumonia or pulmonary œdema are the most frequent.

*Pathogenesis.*—In the somewhat vague condition of our pathological knowledge, the first question which confronts us is whether myasthenia gravis may be classed as an independent disease or no. Kollarits<sup>25</sup> and Raymond<sup>72</sup> would have us believe that most of the reported cases belong to a form of anterior poliomyelitis akin to Landry's disease (some cases of which have given negative results at autopsy), the remaining cases being classified under various headings:—Family affections; cerebral lesions; doubtful cases.

Our study of the literature of the subject has led us to a different conclusion. Though loosely diagnosed in some of the cases, the majority do agree in their main features, which in

combination present a striking clinical picture. Little or no pathological evidence exists of anterior poliomyelitis with which we should expect consistent absence of reflexes and marked wasting, neither of which are features of myasthenia. Under electrical stimuli we should see the reaction of degeneration, and not the myasthenic or fatigue reaction, while the variations and remissions so noticeable in myasthenia would be wanting.

Hoppe and Goldflam† believed that changes in the cerebral cortex were the causative lesions, a view totally unsupported by morbid anatomy. Kalischer and Murri† attributed the disease to changes in the motor nuclei of the medulla, arguing from the similar grouping of the paralyses in some true nuclear lesions, and from the fact that recent hæmorrhages are found in their neighbourhood in cases of myasthenia. No solid histological evidence can be found for this view, which is also contrary to clinical probability. This being so, Oppenheim<sup>8</sup> concludes myasthenia to be either a functional neurosis or a toxic process, explaining the limitation of the changes to certain areas on the ground of a congenital lack of resistance to infective fevers, tumours, etc. The "neurosis" conception is upheld by Massalongo, who terms the disease a motor neurasthenia. Myasthenia indeed possesses many features in common with hysteria, but cannot be regarded as a neurosis if we consider the predominance of motor defects, the presence of paralyses in muscles rarely affected in neuroses, and the character of the electrical reactions. If we adopt the view of a toxic process, which is far the most probable, does it attack nerves or muscles? Against the neurogenic view may be urged nearly all the arguments we have used against anterior poliomyelitis, and also the fact that modern investigators find no typical changes at all in the central nervous system, peripheral nerves, or nerve endings, while such do occur in the muscles. We also have the electrical reactions of the muscles and the analogous fatigue of muscles shown by Bohm after the administration of protoveratrin. Byszowsky,<sup>9</sup> ignorant of the changes to be found in muscle, terms myasthenia a "myositis with no anatomical foundation."

† *Vide* Campbell and Bramwell, *Brain*, 1900.

Buzzard,<sup>82</sup> however, finds muscular changes in all his recent cases, both lymphorrhages and muscular degeneration, and regards them as constant in the pathology of the disease. Their actual significance is doubtful, though Link<sup>49</sup> suggests that the cell nests—"Zellherden"—impede the lymph circulation in its attempts to carry away the products of metabolism from the muscles, which therefore tire much more rapidly. Buzzard, following the views of Botazzi\* and Jotezko,† to the effect that there are two contractile substances in muscle, the protoplasmic and fibrillar, argues from the electrical reactions in myasthenia that it is the excitability of the former which is the more affected by the toxin. That the actual causative toxin is produced primarily in the muscles is improbable, for, as Guthrie points out (*Lancet*, 1901), massage of the muscles once exhausted does not accelerate the return of reaction to faradism.

Furthermore the presence of symptoms apart from those of the motor system—paræsthesiæ, headaches, etc.—testifies to a general toxæmia. The poison is probably not exogenous or microbic, since we do not hear of epidemics or simultaneous affection of two members of a family. From the resemblance of myasthenia gravis to such diseases as Addison's and exophthalmic goitre we believe that it is connected with a disorder of some internal secretion.

Most of the large glands have in turn been suggested as the origin of the toxin. The similarity of the symptoms to the muscular prostration of Addison's disease has suggested the suprarenals, in which, however, no trace of disease has been found, while the administration of suprarenal extract has proved useless.

Guthrie suggests the spleen, arguing from the resemblance of the disease to diphtheritic paralysis and Landry's paralysis. In the former, Sidney Martin has shown that the chief seat of the poison is in this organ, enlargement of which occurs in a few cases of the latter malady, and in three cases of our series of myasthenia. It generally however accompanies some

\* *Archiv. of Anat. and Physiol.*, 1901, s. 377.

† *Journ. de Neurolog.*, 1904, p. 221.

abnormality of the liver, various forms of which are found in six of our cases. Indeed, some authors ascribe the symptoms to a disturbance in metabolism due to disordered condition of the liver. Mohr<sup>43</sup> finds Banti's disease with a puckered liver in a case of myasthenia, and Boldt<sup>110</sup> hepatic cirrhosis in a case of myasthenia in which no history of alcohol was obtainable, whence quoting 'the French view that cases of cirrhosis with no known cause are due to chronic toxæmia by absorption, he suggests that in myasthenia a toxin circulates in the lymphatics which produces an inflammatory reaction in the liver.

Kauffmann<sup>119</sup> investigated the metabolism in two myasthenics and found that during exercise urea provided only 66 per cent. of the total nitrogen in the urine, the ammonia providing almost 9 per cent. of the total, while at rest their quantities were normal. Sulphur also was badly oxidised during exercise. The occasional presence of bile acids and pigments in the urine hinted at hepatic disease. Paralactic acid, formed in consequence of disturbed hepatic metabolism, was present in the blood and in smaller quantities in the urine. Examination of the gaseous exchange showed an abnormally low respiratory gradient in rest and work. No other researches have been made in this direction.

A very interesting connection already discussed appears with diseases of the thyroid gland, which seem to increase the disposition of individuals to myasthenia.

It is interesting to note the especial connection with exophthalmic goitre in view of the persistence of the thymus so often seen in this disease, as also in myasthenia.

In ten of our cases we find abnormalities of the thymus, lympho-sarcomata (Hun,<sup>69</sup> Goldflam,<sup>30</sup> Laquer and Weigert<sup>15</sup>), abscess of the thymus (Burr<sup>73</sup>), and simple hypertrophies (Buzzard<sup>82</sup>). Their occurrence certainly cannot be said to be merely fortuitous, though their exact import cannot be defined with any certainty, since investigation of the physiology of the thymus has up to now not proved very fruitful. Dudgeon<sup>90</sup> obtained merely negative results from grafting thymus intraperitoneally in animals. Svehle however (ref. Zentralblatt f.



allg. path. u. path. anat. nr. 8), has, by giving thymus extract, produced lowering of the blood pressure through injury to the vaso-constrictors, an effect, however, common to the extracts of other organs. He suggests that the sudden deaths associated with enlargement of the thymus are due to excess of thymus secretion in the blood. In this connection we may note that one of our cases which showed enlargement of the thymus was associated with status lymphaticus (Hödlmoser<sup>24</sup>). Injection of thymus extract and sowing fresh thymus under a dog's skin had no effect during life, while after the dog had been killed no cell-nests could be found (Link<sup>49</sup>). Myers<sup>54</sup> cites the experiments of Abelous and Tarelli, the former of whom, after the removal of the thymus in frogs, found weak resistance to fatigue and progressive paresis, the latter, after a similar operation on dogs, a perceptible diminution in the force of the muscular contractions. If the latter results are valid, the toxin of myasthenia may proceed from some disorder of the thymus secretion. The lymphoid deposits in the muscles were at first attributed to metastases from thymus growths, but they do occur in myasthenics, as Buzzard has shown, apart from any pathological condition of that gland. Chvostek has recently advanced the claims of yet another structure, the parathyroids, following Lundborg (Deutsch. Zeitschr. f. Nervenhe., Bd. 27), who suggested that "tetany, paralysis agitans, myoclonus, myotonus, myatonia periodica" form a group of diseases due to disordered function of these glands. Chvostek argues chiefly from analogy with tetany, which he claims to have shown, by experimental and clinical evidence, to have this pathology. Tetany, he points out, throughout nearly all its symptoms, is diametrically opposite to myasthenia gravis in essential points, while both show some common features. In both, only striated muscle is affected and the sphincters are free. But in one, spasm is the chief motor phenomenon; in the other, fatigue. In both the electrical excitability is altered; in the one raised, in the other lowered. In both there is a tendency to combination with Graves' disease. The remainder of his arguments run in a similar unconvincing strain. Investigation into the condition of the parathyroids may well be made at future autopsies. Oppenheim lays stress on the

occurrence in myasthenia of congenital anomalies, several instances of which he records—polydactylia (six fingers), cleft palate, micrognathia, hypoplasia in roots of cranial nerves, doubling of central canal (Senator), doubling of aqueduct of Sylvius, and suggests that congenital diathesis plays a part in the disease. A congenital anomaly in the floor of the fourth ventricle is also chronicled by Frugoni.<sup>118</sup>

#### DIAGNOSIS.

*Hysteria.*—Many cases of myasthenia, I feel sure, have in the past been labelled as hysterical, a serious though pardonable mistake. The distinction is well drawn by Leonard Guthrie (*Lancet*, 1901). In both occur weakness and rapid fatigue, which however differ widely in character. Hysterical weakness generally improves after exercise, and does not disappear after rest. Hysterical ptosis is due to spasm of the orbicularis; myasthenia to paresis of the levator palpebræ. External ophthalmoplegia and lagophthalmos are absent in hysteria. The dysphagia of hysteria shows gulping efforts, followed by regurgitation, liquids being easily swallowed, while in myasthenia there is weakness of deglutition and nasal regurgitation of liquids. In both food may go the wrong way, but in hysteria it is dislodged by a loud cough. Disorder of the speech in hysteria takes the form of whispering, articulation being good unless there is a stammer, unlike the nasal and progressively impaired speech of myasthenics. The dyspnoea of hysteria shows rapid, shallow, and forcible respirations, with occasional overaction of the diaphragm, and no cyanosis. In myasthenia there is real distress, cyanosis, paralysis of the intercostals or diaphragm, weak cough, and accumulations of mucus in the throat. The hysterical patient fails to give the fatigue reaction to electrical stimuli. It is quite probable that some cases of myasthenia get hysterical symptoms superadded which, until death supervenes, obscure the true diagnosis.

*Post-diphtheritic paralysis.*—The ordinary neuritis presents features of resemblance to it in the nasal voice and regurgitation of fluids, ophthalmoplegia externa, paralyses of pharynx, glottis

intercostals, and diaphragm and sudden cardio-pulmonary crises, often fatal. Points of distinction from myasthenia gravis are the absence of knee-jerks, occasional reaction of degeneration, history of sore throat, short duration, addition of ophthalmoplegia externa. A post-diphtheritic chronic bulbar paralysis is described by Harris (Brain, 1905, p. 542), in which occur paralysis of eyes and lips, with weakness of the frontalis and tongue and dysphagia. He points out that it may be distinguished from myasthenia by the absence of ptosis, absence of weakness of jaw and neck muscles, of ophthalmoplegia and myasthenic reaction, and of variability of symptoms.

*Post-influenzal neuritis.*—After influenza, associated with multiple neuritis, we may see ophthalmoplegia, paralysis of soft palate, pharynx, larynx, and cranial nerves, with cardio-pulmonary seizures.

*Chronic bulbar paralysis* is distinguished by the involvement of the lower half only of the face, also by the absence of the electrical reactions and remissions so marked in myasthenia.

*Acute bulbar paralysis.*—*Pseudo bulbar paralysis.*—} Eliminated by the form of development, acute and apoplectiform.

*Bilateral facial paralysis.*—Tongue and ocular muscles (except orbicularis) escape, as also in

*Facial myopathy* in which symptoms are progressive or stationary, not remittent.

*Tabes and cerebro-spinal syphilis* may give some trouble as regards the ptosis and ophthalmoplegia, often incomplete and often the first or chief symptoms. The class of cases of myasthenia in which the symptoms are confined to the eye is frequently confused with the syphilides, especially if the knee-jerk be sluggish (Oppenheim). The pupil however is generally affected in the latter affections, while there are frequently changes in the fundus oculi and myasthenic symptoms are absent. Charpentier<sup>94</sup> records a case in which myasthenia appears to have been super-added to tabes.

*Landry's paralysis* shows a steady progress and a rapidly fatal termination. Electrical reactions are normal. Sensibility is impaired. Superficial reflexes disappear.

*Cerebral tumours*, especially in the basilar region, may present some similarity, but they are to be distinguished by the headache, vomiting, and optic neuritis.

*Addison's disease* resembles myasthenia only in the fatigue.

*Exophthalmic goitre*, as we have pointed out, presents at times similar paralyses, and may be associated with myasthenia in one and the same case.

*Recurrent oculo-motor palsy*.—Rare. A good instance is given by Spiller and Posey.<sup>91</sup> The symptoms begin before the age of twenty-five, with headache, vomiting, or nausea. The headache always stops when paralysis develops, is always the same side, and is termed by Charcot "migraine ophthalmoplegique." The oculomotor paralysis is unilateral and complete (Möbius), though Oppenheim states that it may be confined to one muscle, such as the levator palpebræ superioris. The attacks recur periodically. Post-mortem basal meningitis has been found.

*Vertige paralysant* (of Gerlier) presents interesting points of resemblance. This little-known disease occurs in epidemics. Ptosis is the first symptom; later, paresis of the lower jaw, neck, and extremities, most marked at evening, and in muscles most called into action during the day. A Japanese patient of Miura showed traces of myasthenic reaction. Possibly it may be an epidemic form of myasthenia gravis (*vide* Byschowsky<sup>92</sup>).

#### PROGNOSIS.

Of our 126 cases, 50 are known to have ended fatally, as compared with 23 out of 60 recorded by Campbell and Bramwell. A few recoveries are described. A man (Raymond and Sicard<sup>93</sup>) who suffered from advanced myasthenia—at one time he is said to have resembled a curarised animal—recovered sufficiently to go on a Congo expedition, and at the end of four years was still well. A patient of Raymond and Lejonne,<sup>92</sup> previously helpless, was able to rejoin the Army. Another man returned to work, and had not relapsed at the end of a year (Hoffmann<sup>94</sup>), cf., Ventra,<sup>12</sup> Chvostek.<sup>123</sup> It is so difficult to feel sure that the so-called recovery is not merely a long remission fated sooner or later to relapse. The average duration ranges from one and a half to two

and a half years. The shortest case in our list died after an illness of twenty-nine days (Dorendorff<sup>22</sup>); the longest after seventeen years (Auerbach<sup>32</sup>); eighteen died after an illness of less than one year.

Of our own cases the man's may be called distinctly acute, as it only lasted seven weeks, while the other, who first became ill in September, 1905, in February, 1908, was alive and in fair health.

Attacks of dyspnœa and choking are of grave omen, also the appearance of pulmonary complications. Death may occur with tragic suddenness.

#### TREATMENT.

Treatment is exceedingly unsatisfactory. Improvement or recovery can seldom be traced to it.

The patient should be kept quiet and, if necessary, in bed, warmly wrapped up. Long conversation or effort of any kind should be prohibited, and all excitement avoided.

Slight meals, light and easily digestible, should be taken at frequent intervals. Solids may be taken easier than fluids, as in Dr. Hale White's case. If the dysphagia be severe nasal feeding may be tried, but with great caution, as the tube may bring on a choking fit. Fluids, even when taken by this means, may regurgitate through the nose, and nutrient enemata may be necessary.

The attacks of dyspnœa may sometimes be relieved by tongue traction (Guthrie<sup>124</sup>). Emetics are ineffectual, as in the girl under Dr. Hale White.

As for electrical treatment, faradism does actual harm, while galvanism and massage, though they should be tried, have little obvious effect. Hoffmann's case, however, recovered under galvanisation and strychnine.

As to drugs, iron and arsenic may benefit the general condition. Potassium iodide, mercury and strychnine are apparently useless, also adrenalin.

It is so hard to say whether any improvement in the patient's condition is due to the drug he may be taking.

Thyroid extract given in many cases has not proved of much efficacy, though in Chvostek's case, who also suffered from myxœdema, it cured both sets of symptoms, and in several instances appears to have produced temporary improvement.

The patient of Raymond and Sicard,<sup>83</sup> who appears to have recovered completely, took thymus powder and supra-renal extract in the hospital, but after his discharge took no drugs at all, which raises a doubt as to their share in his improvement. Delile and Vincent<sup>112</sup> claim a good effect for powdered pituitary body and ovary given together.

Note should be taken of the clever contrivance for overcoming ptosis worn by a patient of Mr. J. B. Lawford<sup>85</sup>—a spectacle frame with a wire crutch fitted to the upper part of each eye-piece. These raised the upper lids, and gave great comfort in reading.

Considering the disastrous effect of pregnancy in many cases, marriage is inadvisable for a woman suffering from any myasthenic symptoms.

#### SUMMARY OF CONCLUSIONS.

*Etiology.*—The proportion of males to females is a little higher than 1 to 2. A fair proportion of patients have followed sedentary occupations. Myasthenia gravis in some cases follows on emotion, overwork or infective fevers. It may be associated with diseases of the thyroid gland, especially exophthalmic goitre, and also with pregnancy and lactation.

*Clinical features.*—At the onset we most commonly find headache and paresis of the external eye muscles. Unexplained ptosis should always make us think of myasthenia.

When the disease has developed we see rapid fatigue associated with some degree of constant paresis or paralysis of special muscle groups especially those innervated from the bulb, those of the face, eyes, tongue, pharynx, jaw. Speech at first normal soon becomes nasal and finally unintelligible. Strabismus appears after the patient has gazed at some object. Internal ophthalmoplegia is rare, though in a few cases fatigue of the pupil or hippus is found. The tongue can only be protruded a few times. The neck muscles after a short time

fail and allow the head to droop. The muscles of the limbs and trunk are generally affected in some manner, and occasionally the diaphragm and heart.

Attacks of dyspnœa and dysphagia occur, and may end in sudden death.

There is a peculiar fatigue—"Erschöpfung's"—reaction of the muscles to faradic stimuli which on repetition soon fail to elicit any response. The knee-jerk is often somewhat exaggerated, and fails more or less after several taps.

Remissions and variations are characteristic of the disease. Symptoms are worse after exercise or emotion, and better after a short rest. They may be absent in the morning and only appear as the day goes on, nearly always reaching their height in the evening. Disorders of sensation do occur in some instances, as also localized atrophy, though this was denied by earlier observers.

*Morbid anatomy.*—Muscular changes are the most certain phenomena, *i.e.*, lymphoid deposits and early degeneration. They may appear conjointly with changes in the thymus, persistent simple hypertrophy, sarcoma or abscess. Inconstant minute cerebral changes are described, chromatolysis in bulbar nuclei, and small hæmorrhages, probably terminal. Some cases show hepatic disease. Pneumonia or bronchitis is common as the actual cause of death.

Numerous views have been put forward as to the origin of the disease, *e.g.*, that it is due to an anterior poliomyelitis, to changes in the cerebral cortex or in the bulbar nuclei; that it is a motor neurosis.

*Pathogenesis.*—It is most probably due to a toxin produced by some disordered internal secretion and acting on the muscles. The source of the toxin cannot be definitely ascertained, the liver, spleen, thyroid, thymus, and parathyroids being accused in turn. The lymphorrhages may act by blocking the outflow of fatigue products, or may be mere local manifestations of a general toxæmia.

*Prognosis.*—Generally bad. Recoveries are said to occur, but they are difficult to distinguish from long remissions.

*Diagnosis.*—Chiefly from hysteria, cerebral syphilis and tabes, post-diphtheritic paralyses, and chronic bulbar paralysis.

*Treatment.*—Little more than rest, quiet, warmth, tonics, careful feeding. Nutrient enemata may be necessary. In some cases thyroid extract appears to have done good. Extract of thymus or ovary may also be tried.

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## ABSTRACT OF 124 CASES.

(The numbers given correspond to those of Bibliography.)

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Schüle.

1.—Woman, æt. 23. Onset in February, 1896, with pains in limbs. In June, nasal voice, dysphagia, nasal regurgitation of fluids. Bedridden. August, weakness of legs, later of arms. Condition on admission to hospital August 30th, 1897:—Bronchitis. Apical systolic murmur. Pupils react normally. No facial palsy nor external ophthalmoplegia. Speech weak and nasal. Weak ineffective cough. Movements of limbs weak. Muscles of neck and trunk unaffected. No atrophy or fibrillary twitching. Knee and tendo Achillis jerks not brisk. No disturbance of sensation, mental condition, or of sphincters. September 4th, 1897. Sudden dyspnoea. Death in three hours. Post-mortem.—Small warty deposit on aortic valves. Liver fatty. Central nervous system: Microscopically, numerous grey discolourations, the size of a millet seed, near the "olive." Small recent hæmorrhages in bulb at level of tenth nucleus.

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Hall, A. J.

2.—Mrs. X., æt. 44. Multipara. Nervous stock. Has had migraine. Domestic worry of late. General muscular weakness in December, 1906. Always tired. About Christmas some swelling left side of face and ptosis left eye, which recurred during day and increased towards evening. In February took to her bed. Ptosis both eyes. Variable irregularity of ocular muscles. Hands feeble. Can only occasionally sit up or stand. No wasting or loss of sense. Tendon and superficial reflexes normal. Speech slow and feeble. Difficulty in swallowing. Electrical reactions normal. Much worse after temporary improvement in March. General weakness much increased, especially if attention be called to it. Much depression. Voice nasal. Slight attacks of dyspnoea in morning. Sudden fatal respiratory failure April 2nd, 1897. Nothing found abnormal in brain or medulla micro- or macroscopically.

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Guastoni and Lombi.

3.—S. P., æt. 33, Jew. Onset October, 1896, with weakness in arms and variable ptosis right eye. In November admitted Hosp. di San Spirito. Difficulty in continued mastication and deglutition. Transitory diplopia worse at night. February, 1907, ptosis left eye. Tongue tremulous. Arms can never be raised completely, and not at all if attempts be repeated. Legs weak. Can only stand erect for a short time. Reflexes normal. Some superficial formication. Reaction of muscles to faradism soon ceased, though normal to galvanism. In March feverish attack. May, much temporary improvement. Mastication perfect. Discharged in 1899, general weakness and myasthenic reaction still existing.

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Paul.

4.—A. P., æt. 23 (female). Onset eighteen months after confinement. Unable to rise from stooping posture. Difficulty in climbing stairs. Next, transient weakness in arms; hands tired. Transitory diplopia. Expressionless face. Voice occasionally nasal. Words ran together. Occasionally

swallowing awkward, and neck muscles gave way. Symptoms became more frequent and serious. She choked in swallowing water. Occasional palpitation and dyspnoea. Sphincters and sensation unaffected. At times could not roll over or sit up in bed. Knee-jerk normal. Electrical examination omitted. No atrophy. Remissions occasional. On one occasion worse for cold. Death eighteen months after onset. At autopsy nothing found macroscopically.

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S. Brown.

5.—Miss A. B., æt. 29. Teacher. Good health previously, though slightly nervous. After several months, during which she attended an unusual number of social functions involving loss of sleep, she complained of feeling muscular exhaustion in arms and legs following exertion. Diplopia and ptosis soon troublesome, the former aggravated by sunlight. Soon, nasal voice. Speech natural at first; after talking short time became thick, and then exhausted. Mastication soon tired. Occasional palpitation. Slight tinnitus. Frontal headache and pains at side of body. Hair fell out. Constipation. No mental symptoms, abnormality of reflexes, or atrophy. After four months' rest became better for a few weeks. Electrical tests not made. Sixteen months from onset condition had not much altered.

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De Buck and Brœckaert.

6.—Female, æt. 30. No history of infectious disease, or syphilis, or nervous heredity. Onset in May, 1900, with difficulty in speech. Easily tired in mastication and ocular movements. Difficulty in deglutition. Nasal regurgitation of food. Frequent sensation of suffocation. In December, 1900, nasal voice. Weakness of neck muscles. Unable to completely close lids. Slight bilateral ptosis. Marked asthenopia. Intermittent diplopia. Pupils react normally. Sensation of palate and pharynx unaffected, also movement of laryngeal cords and reflexes.

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Giese and Schultze.

7.—Married woman, æt. 24. In May, 1899, had a cough and occasional headache, usually right-sided. Diplopia improving after ten days under electrical treatment. At the end of May difficulty in speaking and swallowing, with nasal regurgitation. Fatigue right side of jaw. Weakness of tongue. June, 1899, diplopia returned, varying in degree. Middle of June, right ptosis. Movements of thumb, second and third fingers of both hands failed after exertion. Burning sensation along median nerve. Movements of head and arms, especially left, weak. August 23rd, complete aphonia. September 2nd, slight cervical scoliosis. Fundus oculi normal. Paresis of orbiculares oris and palpebrarum. Palate, both sides paralysed, right side completely. Right upper limb partly paretic, left ilio-psoas paretic—no atrophy or fibrillary tremor. Vocal cords feeble, especially in abduction. No myasthenic reaction or reaction of degeneration. Liver edge palpable. Treatment, rest in bed, Pot. Iod., Iron, Faradisation. September 11th, right ptosis disappeared, to reappear on the 14th, when there occurred a dyspnoic attack. Diaphragm apparently useless, loud tracheal râles, weak respiration, feeble cough. Better September 17th. October 3rd, no clonus to faradism in orbicularis palpebrarum. Slight reaction of degeneration in

right levator palpebrae superioris October 9th, patient cannot wrinkle forehead. October 23rd, great dyspnoea. Complete paralysis of muscles of speech, deglutition, and mastication. 24th, death. Post-Mortem.—Skull cap very thick. Examination of brain negative.

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Oppenheim.

8.—Woman, æt. 48. Employed in domestic agency. For six years, shortness of breath, palpitation, hand tremors. Diplopia for a few weeks in 1896. Now (August 20th, 1907) complains of loss of sleep and appetite, irregularity of bowels, polyuria, and hyperidrosis. Pulse very rapid. Tremor of hands much increased by active movement. Tendon reflexes exaggerated. Diagnosis: "Morbus Basedowii." October, 1897, difficulty in speaking and swallowing, slight ptosis, and inability to close eyelids. Speech nasal after talking. Swallowing difficult. Palate moves well. Pulse 90-96. Arms strong. Inability to completely extend middle and end phalanges of second and third fingers. Electrical reactions normal (myasthenic reaction appeared later in extensors of fingers). November 28th, 1898, great weakness. She can neither whistle nor blow out a light. Soft palate feeble. Diaphragm feeble. Respiration slow and shallow. March 23rd, 1899, attack of severe dyspnoea, lasting two hours. Ptosis marked. Nearly complete paralysis of orbiculares palpebrarum, and oris. March 26th, exhaustion and cachexia. Dyspnoea. Paralysis of muscles of swallowing and diaphragm. Death. Post-mortem: Unimportant recent hæmorrhages in brain cord, nerves, and muscles.

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Kurt Mendel.

9.—Serving Maid, æt. 21. Strong tuberculous family history. In February, 1900, following a fright, difficulty in speech, and swallowing. Tinnitus especially towards evening, when general condition was worse. General weariness. Occasional nasal regurgitation of food. Frequent cramps in calves at night. July, 1900. For a short time attacks of loss of consciousness while remaining in standing posture. January, 1901. Weakness of eyelids, especially right, and of lower part of face. Both recti interni soon tired, failing to keep axis of eyeballs straight for long at a time. Pupils oscillate in response to light (hippus), while their contraction, at first good, soon fails. Except on rare days no movement of palate in phonation. Voice after a few words rapidly becomes indistinct. Arms often can only be raised four or five times. Whole right side of body apparently more sensitive to prick than left. By the X-rays contraction of diaphragm seen to soon tire. Pulse good, though it occasionally dropped a beat, especially in the evening. Spleen occasionally palpable. Blood normal. Urine, trace of albumen. Hyaline and granular casts. Myasthenic reaction, at first absent, obtained 11th January, 1901. No reaction of degeneration. Eleven months' history.

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Déjerine and Thomas.

10.—Female, æt. 58. In 1891, after domestic trouble, speech became slow and difficult. Hearing impaired. May, 1894, voice slow and nasal. Movements of tongue slow. Paresis of lip, and in some degree of laryngeal adductors. All reflexes normal except the pharyngeal reflex, which was absent. Face expressionless, bilateral ptosis. Inability to whistle. Mouth

partly open with saliva dribbling. Left labial fold deeper than right. Patient emotional, laughs or cries. Eyes cannot be completely shut except in sleep. When she wakes, she has to raise the lids with her finger. Eye movements, bite, and rotatory muscles of neck weak. Some feebleness of upper and lower limbs. Slight atrophy of thenar eminence both sides, probably due to some arthritis of carpo-metacarpal joints. Slight diminution in excitability to faradism. With some variation in degree the symptoms in general increased, till death from pneumonia in March, 1896. For Autopsy see p. 78.

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Buist and Wood.

11.—Mr. E. R. R., æt. 34. Since 1892 occasional pains in legs and feet, restlessness of feet at night. In February, 1900, ptosis left eye, partly recovering in three weeks. April, occasional diplopia. June, loss of power in left arm. Occasional attacks of tingling all over, with feeling of oppression in chest and stomach. July, loss of power right arm, then weakness of lower limbs. No trouble with sphincters. November, partial double ptosis and partial external ophthalmoplegia. Lips weak and easily tired. Tongue, protruded well at first, soon quivered, and in two minutes fell back. Jaw muscles and grip feeble. Deltoids flattened and small. Expansion of chest by deep inspirations soon diminished. Lower limbs weak. Reflexes normal. Myasthenic reaction in biceps and deltoid. No sensory disturbance. Pulse 76-88. Temperature 98.6-99° F. November 29th. Some difficulty in swallowing. Nasal regurgitation once. Muscular power improved while under observation, *i.e.*, till December, 1900.

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Ventra.

12.—Male, æt. 38. After attack of rheumatic fever sudden onset of general weakness with double ptosis. In November, 1897, temporary improvement. Monthly variation. When he came under notice in September, 1898, could walk, but soon tired. Divergent strabismus came on. Tongue tremulous after it had been kept out some time. Speech nasal after ten minutes. Deglutition difficult. Myasthenic reaction. After a month's treatment with thyroid improved sufficiently to return to his occupation of sailor.

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Bramwell.

13.—First case recorded in Scotland. Female, æt. 23. Single. Seen first on November 10th, 1900. Health good. Ten weeks before, difficulty in speaking noticed on return from holiday. Speech natural on rising in morning, became worse and nasal at end of day. Lips became stiff and unmanageable. Saliva ran from mouth at night. Nasal regurgitation of fluids. Jaws tired in eating, arms in brushing hair, and hands at the piano. Neck weak. Attacks of breathlessness, worse on excitement. The use of any muscle seems to tire the others. Not emotional. No ptosis. Reflex irritability of palate diminished, especially on left. Myasthenic reaction in right biceps. Deep reflexes well marked. Plantar reflexes flexor.

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Burr and McCarthy.

14.—Female, æt. 19. Unhappy married life. January, 1898, abortion, probably induced. A year after, subjective numbness, hands, legs, and back. Sensation to touch, heat, and cold unaffected. April, 1899 rapid onset of

weakness in arms and legs. Difficulty in walking. Dynamometer, fifty in each hand. Knee-jerk exaggerated and easily exhausted. Exaggerated elbow jerk. No ankle clonus or Babinski's sign. Slight tremor, hands, head, and eyelids. Drooping of eyelids. Tongue tremulous. April, 1900, though she could lift head it drooped forward. Face expressionless. Could not wrinkle brows. Speech weak. Eating tired her. General languor. Slight constant choreiform movements of face and arms. No muscular atrophy. Difficulty in swallowing. Vision in each eye reduced one-half to one-third. Extrinsic ocular movements much impeded, especially outward. Ataxic movements of eye. Lids cannot be closed. May 13th, dysphagia. Sudden dyspnoea. Pulse rapid and weak. Cyanosis, coma, death. For post-mortem findings, see p. 79.

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Laquer and Weigert.

15.—Locksmith's assistant, æt. 30. No history of syphilis or alcohol. In 1896 and 1897, attacks of giddiness, palpitation, and fainting. Married in 1898. Fatigued after coitus. Pains in head and body. In June, 1900, arms weak. July, right ptosis. August, slight left ptosis. Muscles of jaws and throat rapidly exhausted. Voice quickly got hoarse in reading, and fell in pitch in singing. Deltoids readily exhausted. The muscular paresis worse at evening. An experimental exhaustion of muscles by voluntary movements induced temporary cardiac failure. Pulse fell from 72 to 40. Treatment, rest in bed, iodides, and arsenic. In four months he returned to work, having gained twelve pounds in weight and lost much of fatigue. Symptoms recurred in a month, with paresis of muscles of tongue, deglutition, neck and trunk. Nasal voice. Bedridden. Left pupil larger than right. Frequent attacks of collapse. Myasthenic reaction. In February, 1901, paresis of intercostals and diaphragm. Death, February 6th. For post-mortem, see p. 79.

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Risien Russell.

16.—Male, æt. 57. Good health till eleven months ago, when "blood poisoning," necessitating amputation of right index finger. Has not been strong since. Five months ago his legs gave way under him when walking, letting him fall. Since then weakness has been progressive. After walking short distance, legs begin to feel numb, knees give way, and he falls, but on being assisted to rise can resume walking. Eyelids drop at times. Sees double on looking to left. Speech becomes more and more difficult to understand during conversation. Difficulty in chewing and swallowing. Liquids occasionally regurgitate through the nose. Attacks of dyspnoea and faintness. Symptoms vary; always worse after effort. Bilateral ptosis; skin of forehead unduly wrinkled. On looking up for a short time wrinkles disappear from fatigue, and ptosis increases. Pupils react to light and accommodation; not fatigued by prolonged effort at latter, or long exposure to bright light, under which condition they oscillate. Slight nystagmoid movements. Convergence defective. Cannot close eyelids tight, pout lips, or whistle. Tongue tremulous, not atrophied, kept protruded with difficulty, and readily fatigued in all movements. Palate fatigued by repeated vocalization of letter *a*. Voice soon tired by reading, blurred and nasal. Can only keep arms raised above head a few seconds. Grasp feeble in both hands, and gradually relaxes.

Expansion of thorax poor; effort at forced movements soon causes considerable embarrassment. Flexors of hip and adductors of neck weak and easily tired. No muscular atrophy. Myasthenic reaction in many muscles. Knee-jerks unduly active, not to be exhausted. No ankle clonus, plantar reflex flexor. Sphincters and sensation normal.

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Long and Wiki.

17.—Tailor, æt. 46. Admitted to Geneva Hospital for bronchitis. Thin, weak, somewhat dyspnoic, with fine râles both lungs. No disorder of nervous system noted. Returned to work much better. July, 1899, onset of great weakness, arms and legs. Leaving work he re-entered hospital. August 5th, pulmonary condition as before. Marked feebleness and rapid fatigue. Head cannot long be held upright. Pains all over. Tongue and voice normal. Cannot whistle or puff out cheeks. Pupils very inactive. Mastication weak and painful. Deglutition difficult. Paresis of both arms, which tremble and rapidly tire at slightest effort. Lower limbs vary. He finds it difficult to get out of bed, and then, after a few steps, falls. No trouble with sphincters or sensation. No atrophy. Deep reflexes exaggerated. Condition stationary till October 22nd, when dyspnoea came on with cyanosis. Death in two hours. For abstract of autopsy, see p. 79.

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G. Von Wayenburg.

19.—Woman, æt. 35. Remarkable expression. Half shut, fixed eyes; mask-like visage. Head bent forward and supported by hand. Air of intense fatigue. Almost complete external ophthalmoplegia (system of left "abducens-externus" still movable). Paresis of both levatores palpebræ superioris. Immobility of middle facial muscles. Chewing muscles powerless. Swallowing difficult. Tongue protruded well. Variations in difficulty of swallowing, and paresis of extremities. In the morning she can eat food, and raise hands and arms, both of which are impossible by mid-day. Electrical reactions, fundus oculi, bladder, and rectum normal. No myasthenic reaction. Reflexes brisk. Two attacks of dyspnoea while under observation.

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Hogg, C. H.

20.—Miss —, æt. 37. Attacks of mild tonsillitis. A slightly enlarged tonsil removed. Business worry. In December, 1905, slight difficulty in swallowing fluids. Nasal regurgitation. Weakness of accommodation. Anæmic, nervous, quick pulse. After a week, temporary improvement till middle of January, when relapse occurred. In February, weaker, occasional faintness, shortness of breath, difficulty in moving little finger, slight weakness in legs. Paralysis of soft palate. Slight ptosis, right eye. Pulse quick, feeble. Next day ptosis gone, to return three days later with slight paresis of frontalis and corrugator supercilii and, later, of externus rectus, orbicularis palpebrarum, risorius and zygomatici. Weakness of tension and adduction of vocal cords. Occasional coughing and choking attacks. Treatment, electricity, massage, etc. Attacks of dyspnoea. Swallowing impossible. Feeding by tube caused dyspnoea and faintness. After a second rally, during which swallowing power improved, a relapse occurred. Temporary loss of power to move tongue. Fatal dyspnoea. Death in (?) March, 1906.



## Priszner.

21.—Peasant woman, æt. 36. May, 1901, appearance of difficulty in swallowing, salivation, indistinct speech. General weakness. Let light objects drop. Symptoms slight in morning. Four years previously there had been left ptosis and defect of vision left eye, improving after a few weeks' electrical treatment. The last two years she has noticed fatigue after work, and that she had to exert herself to speak and swallow. Slurring of speech. Ptosis recurred on the left side and appeared in slight degree on the right side. Having previously worked hard she now was scarcely able to do house work. Frequent temporary improvement lasting from hours to weeks. Condition in May, 1901:—Muscles of neck and upper arm are wasted and feel like thin cords. Thenar and hypothenar eminences flat. Abdomen hollow. Pulse 96, small, feeble. Weakness of facial muscles. Wrinkled forehead. Nasolabial folds shallow. Mouth half open. Drowsy expression. Protruded tongue soon drawn back, tremulous. Speech nasal. Knee-jerk weak. In July, great improvement, housework resumed. January, 1902, relapse. Choking attack. Pulse 104. 11th January, fatal attack of suffocation and respiratory failure.

## Dorendorff.

22.—Merchant, æt. 27. Twenty to twenty-five glasses of beer daily. History of diphtheria, gonorrhœa, and syphilis (in 1901) from which apparent complete recovery under mercury. April 7th, 1902, sudden diplopia and right ptosis. 9th, weakness and tiredness in legs, later in arms. Frequent falls. April 14th, left eyeball could not be turned in any direction, all efforts only resulted in a twitching. No abnormality of lens or reflexes. Weakness in walking. April 20th, facial paralysis. Weakness of neck muscles, and erector spinæ. To sit up turns on to side and draws himself up by hands, which themselves rapidly tire. April 21st, difficulty of mastication after first two minutes. Lips and voice tired. Cannot count one hundred. Myasthenic reaction in chest muscles, rectus abdominis, and limbs. April 26th, difficulty in defæcation from insufficient abdominal pressure. Blood and urine normal. After remissions and exacerbation, sudden death on May 4th after twenty-nine days' illness.

## Reneki.

23.—Female, æt. 27. First symptom, diplopia following blow on neck, lasting one day only, but recurring later to last three weeks. Then ptosis, difficulty in chewing. Four weeks after blow onset of bilateral weakness of upper and lower limbs with very rapid fatigue. Daily variations in degree. Condition when first seen: Bilateral ptosis. No atrophy. Eyelids can be strongly closed. Eye movements very limited in all directions. Nystagmus. Reaction of pupils to light soon exhausted. Exhaustibility of muscles of neck and limbs. Myasthenic reaction both limbs. Knee-jerk and sensation normal. Blood count normal. Further course: Difficulty in swallowing; chewing worse. Occasional diplopia. Gradual improvement in two years.

## Hödlmoser, C.

24.—Maid servant, æt. 18. Overworked. No nervous family history. October, 1898, when carrying a basket one day noticed she could carry it no

longer, while at one and the same time left eyelid drooped partially over eye and she saw everything double. Condition lasted an hour, when it completely disappeared to return in eight days. Seen in October, 1898, decreased corneal and palate reflexes, and increased knee-jerk noted. Slowly increasing weakness of upper limbs. Ordered Tr. Valerian. After speaking some time speech failed and she could only move lips and tongue with difficulty. Muscles of chewing easily tired. She had to support lower jaw with hand. Difficulty in swallowing. Frequent nasal regurgitation. Difficulty in writing increasing with exercise. Attacks of diplopia and ptosis more and more frequent. Condition on admission: Nutrition good. Complete left ptosis. Tongue, slight tremor, put out well at first but soon has to be drawn back. Chewing muscles soon tired. Speech nasal and exhaustible. Whistling and puffing out cheeks impossible. In the act of laughing face is at first normal, later mask-like. Palate reflex decreased, other reflexes normal. Slight paresthesia of upper limbs. Right hand tires before left. Muscular contractions after a time are reduced to a fine tremor. Lower limbs free. Myasthenic reaction in left side of face and muscles of forearm. Ptosis increases with a fixed stare at anything. Divergent strabismus. Ocular movements limited in all directions, especially to left. When eyes are turned out as far as possible, vertical nystagmus appears, first slow, soon quicker. February 22nd, disappearance of nearly all symptoms. 24th, tinnitus left ear. 28th, pains in legs. March 8th, urticaria. Diplopia previously absent. 10th, the only muscular movements now limited are those of arms. 27th, pains over loin. April 4th, definite improvement after daily galvanism. May 16th, dysphagia, constipation. Pains in arms. Sudden heartache and dyspnoea for half an hour. Vocal cords sluggish, glottis incompletely closed. May 29th, headaches, nasal speech. In spite of temporary remissions general condition grew worse till March, 1900. Dyspnoea. Movements of eyes up and to the left limited. March 9th, much worse. Pulse 140-180. Cyanosis. Respiration first slow (twelve per minute), then "Cheyne-Stokes." Death. Post-mortem.—Status lymphaticus, *vide* p. 79.

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Kollarits, J.

25.—(1). F. L. W., Jew, æt. 48. Phthisical family history. Mother had migraine. Onset in December, 1898, with weakness and unintelligibility of voice. Sudden temporary recovery in February, 1899, on electrical stimulation. Worse after warm baths. Condition much the same till June, 1900. Difficulty in swallowing. Nasal regurgitation. General weakness, inability to rise from chair. Tired after twenty steps, but went on after a rest. Muscles exhausted by both faradism and galvanism. Muscles of chewing, upper and lower extremities, weak and easily tired. Worse in evening than in morning, when voice quite clear. No marked change till January, 19th, 1901.

(2). Jewish seamstress, æt. 32. One son bled to death after circumcision. Onset of illness in 1892, with weakness of extremities (at first of right more than left), and of diplopia, worse in evening. Sudden attacks of tiredness, with dizziness and headache. Slight improvement till relapse one and a-half years later. The two sides of body now affected equally. Speech difficult. Several sentences caused alarming dyspnoea. Difficulty in chewing and swallowing. Nasal regurgitation. In 1898 ptosis right eye,

later of left; variable, and always associated with fatigue of extremities of same side. Always worse during menstruation. Admitted to hospital, August, 1898. Right side of thyroid large. Eyes almost fixed. 1899, improvement in bed. Left nasolabial fold flattened; later, both. Reaction to fatigue very marked under both faradic and galvanic stimuli. No reaction of degeneration. Pupillary reaction to light and knee-jerks lessen with fatigue, but do not disappear.

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Liefmann.

26.—Girl, æt. 19. Diphtheria five years before. Early in 1898, left-sided facial paralysis and ptosis. Improvement under electrical treatment. Since August, 1899, double facial paralysis, paralysis of lids. Difficulty in speech and swallowing. Partial external ophthalmoplegia. Slight external strabismus. In September, 1899, mask-like face. Speech, clear at beginning, is nasal and indistinct at end of first sentence. Slight fibrillary twitching of tongue, which shows slight atrophy of right side. Weak temporal and masseter muscles. Right knee-jerk only obtained occasionally and with difficulty. Right Achilles jerk absent. Sensation normal. No contraction of orbicularis oris, zygomatici, and frontalis to faradism, and weak contraction of frontalis to galvanism. Anæmia. Hæmic bruits. Laryngeal cords not fully approximated. Great variation of symptoms. Inability to hold jaws closed for long. December 18th, twenty-two months after onset, sudden fatal dyspnoea.

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Raymond, F.

27.—Male, æt. 43. From 1895—99 some trembling of right hand, which ceased when he gave up alcoholic habits. August, 1901, suddenly noticed he rapidly tired in reading and writing. Then diplegia. Treated with mercury. Eight days later, weakness of limbs. Symptoms progressed for four months, then became stationary. No trouble with voice, sensation, reflexes or sphincters. No atrophy. Upper limbs stretched out with difficulty soon fell. To rise from supine position he would roll on to side and try to get on to knees. Good response to faradism and galvanism. Up to January, 1902, condition almost stationary. Slight temporary improvement under suprarenal extract.

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Down, E. A.

28.—Male, æt. 23. No history of syphilis. Onset ten months before examination with uncomfortable sensations in head, followed by ptosis. Articulation perfect when starting conversation, soon became thick, while patient felt unable to control tongue. Difficulty in mastication and deglutition. Last few months "cramps in throat" during swallowing which cause nasal regurgitation. When trying to swallow he has to incline head to left. Tongue tremulous after few minutes' protrusion. Paralysis right half of soft palate. He plays the harmonica, but after a few minutes has to desist because air passes through nose instead of mouth, to prevent which he closes the nostrils with thumb and finger or a spring clip. Respiratory muscles soon exhausted, but regain power by rest. While walking or standing he drops suddenly helpless for a spell. No loss of consciousness or sensory trouble. Symptoms occasionally absent for several weeks. Myasthenic reaction. No atrophy. Lagophthalmos.

Patrick, H. T.

29.—Negro (not pure), æt. 25. Five years ago weakness of arms with a dull ache and feeling of intense fatigue. Symptoms relieved by short rest. Gradually worse. Unable to do work for three years. General myasthenia present, very much increased by short activity. Muscles of eyes, face, mastication not vigorous, but no weaker than those of extremities. Myasthenic reaction present in limited degree, and deep reflexes, when elicited twenty times, showed some exhaustion. No bronzing.

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Goldflam.

30.—(1) Male, æt. 27. Development of paralysis in two weeks—first arms, then thigh and trunk (especial involvement of cervical and abdominal muscles). Later, fatigue in chewing. Threatening collapse, with dyspnoea. The parts of the extremities nearest to trunk the most affected. Rapid fatigue. Recovery of functions after rest. Voice weak. Paresis of lower part of face. Symptoms very variable. When they were at their height knee-jerk was exaggerated, becoming sluggish as they disappeared. Patient's knee-jerk could be tired a little. Stinging, burning pains in neck and interscapular region. Electrical reactions normal. Improvement so great that after six and a half months he was discharged from hospital. One month later bad relapse, followed by gradual recovery. In July, 1903, no lack of power could be discerned, and no abnormal symptoms except the sensations of stinging and burning. In December, 1903, sudden relapse. Right ptosis. Weakness of muscles of expression. Head movements weak. To rise from lying down he had to clasp his legs. Weak contraction of diaphragm. Head sunk forward. January, 1904, inability to open mouth. Death on 5th September, 1904, from respiratory paralysis. No cyanosis.

(2).—Frau B., 32. Came for facial hemiatrophy. Infantile uterus. Menstruation normal. From early youth had prominent eyeballs and small goitre. Left-sided facial hemiatrophy had gradually come on during last six years. Movements, sensation, and electrical reactions of face unaffected. In July, 1900, appearance of left ptosis and slight lisping in speech, improved by electrical treatment. In October, left pupil a little smaller than right, and with hemiatrophy showed paralysis of sympathetic. Patient became oppressed. Traces of sugar in urine. Severe pains in left leg. 7th March, 1901. Voice nasal. Nasal regurgitation of fluids. Great feeling of weakness, especially of arms. Difficulty in swallowing solids. Feeling of foreign body in throat. Muscles of expression all very weak. Fibrillary twitchings of tongue when stretched out. Soft palate moves weakly. Voice soon unintelligible, recovering after rest. Reflexes and sensation normal. 8th March, 1901. Nasty cough, with inability to bring up phlegm. Contraction of diaphragm poor. Myasthenic reaction in biceps, not in face. 9th. Suffocating attack repeated next day with loud rattlings on inspiration. Pulse 90. Prostration extreme. Albuminuria. Cyanosis. Pulse 130—irregular. Death 11th March, 1901.

3. (Case 5 of his series).—Overworked seamstress, æt. 30, attributes disease to grief. Seven years before had bilateral ptosis and general weakness, which gradually improved with electrical treatment. Health good at marriage two and a half years ago. Bore a child which she suckled ten months. Then

had a nervous attack, thought to be hysterical, and similar to one suffered seven years before. Onset of ptosis, diplopia, difficulty in speech and swallowing. General weakness. Seen 12th March, 1907. Pale thin woman. Mask-like face. Bilateral ptosis, worse after attempts to raise lids. After reading, muscles of convergence tire (right before left) and diplopia ensues. Lips cannot pout. Rapid tiring of mastication. Swallowing slow. Occasional nasal regurgitation. At end of a meal a piece stuck in her throat. Speech much worse after eating. At first clear, soon nasal. A draught of cool air makes speech worse, lips and fingers stiff. Arms weak and easily exhausted by lifting. Legs tire in walking, knee-jerk active, no ankle clonus. Glutei weak. Myasthenic reaction in several muscles. 29th May, 1901, slight fibrillary twitchings of orbicularis oris and palpebrarum. June, 1901, went away three months to country. Rapid improvement. In September gain of nine pounds in weight. No diplopia or ptosis except when out in street. Insomnia troublesome. A small swelling on cricoid thought to be an aberrant thyroid gland. 5th October, 1901, better, can walk further. Sleep good. 10th October, 1901, relapse, symptoms generally worse. Treatment.—Thymus substance given in second half of June, after improvement had set in. No definite result. N.B.—Pieces were cut out of left deltoid and examined histologically with no result.

✓ 4. (Case 6 of series).—Boy, æt. 4½. In August, 1900, appearance of ptosis associated with low spirits. Recovery in four weeks after use of salt baths. March, 1901, recurrence of ptosis. Lips did not close well and allowed food to escape. Patient had to support lower jaws. Speech indistinct. Tonsils being rather large were cut out, with no subsequent improvement. Nasal regurgitation. The boy played with his mates, though not so cheerful as usual. Often has sore throat. Has epileptic relations. On admission to hospital appears a well-developed boy. Bilateral ptosis (left more), worse when he gazes at objects. No squint, diplopia, or abnormality of pupils. Cannot whistle, which he formerly did. Facial movements somewhat weak. Voice nasal, though soft palate reacts well. Symptoms absent in morning. Rest of body sound. Slight myasthenic reaction in deltoid and extensors of left forearm. Electrical reactions on face foiled by resistance of patient.

5. (Case 7 of series).—Synagogue singer. Male, æt. 61. One year ago noticed loss of clearness of voice, lasting only a short time, but recurring later in speaking as well as in singing, and becoming nasal. Feeling of tightness in throat. Difficulty of swallowing, especially solid food. When seen, May 20th, 1893, is well built. Soft palate motionless to mechanical stimuli and in phonation. No jaw reflex. Tongue small, trembles a little, weak in movement. Lip muscles weak. Nasal voice. No myasthenic reaction. August 11th, 1893, some improvement, increasing as winter came on. Voice clear in singing, except after long effort. Soft palate moves fairly well in phonation. December 12th, 1893, worse. Orbicularis palpebrarum weak. Difficulty in swallowing. January 22nd, 1894, pain in neck. All movements strong, except shutting eyelids. December 11th, 1894, recurrence of old symptoms plus weakness of facial movements. Passed out of observation, and actively followed his calling, till death in February, 1901. Post-mortem.—Mediastinal tumour and lympho-sarcoma of thymus.

6. (Case 8 in series).—Woman, æt. 35. Seen in summer of 1896. Five weeks before Easter woke up with dizziness and darkening of visual field,

while drooping of upper lids appeared in the course of same day. Later, diplopia and micropsia. Two weeks after Easter, weakness in arms and legs. Voice nasal and soon tired. Trouble in swallowing; feeling of foreign body in throat. Nasal regurgitation of fluids. Has had much trouble in nursing sick child. Has had two children, and is two months pregnant. Bilateral ptosis. At times lids can be raised, but soon fall. Diplopia on looking to side. Movements of soft palate soon become feeble. Extremities somewhat weak. Left knee-jerk weaker after repeated taps. Marked myasthenic reaction. Eye condition: Oculo-motor paresis both sides; abducens paretic; right eye ptosis; paresis of accommodation, both eyes; dilated left pupil. Vision: right, one-tenth; left, one-sixth. On July 1st, 1896: right, one-fourth; left, one-third. General improvement. Went back to work well except for ptosis and diplopia. October 27th, 1901, five years later: Marked relapse. Weakness of legs and arms and speech. Dysphagia. Nasal regurgitation. Pale and thin. Eyelids and facial muscles and tongue weak. Neck feeling flaccid. Myasthenic reaction.

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Gowers, Sir W.

31.—(1) Girl, æt. 23. Well till 21, when symptoms set in, slowly increasing till seen two years later in 1894. Stiff look of eyes and absence of natural smile, which was only represented by elevation of upper lip, with no outward movement of angle of mouth, *i.e.*, no action of zygomatici or risorius. This results in a "nasal" snarl. Slight ptosis, especially on left. Movement of left eye out and in reduced to one-eighth of an inch; right could not be moved out; both moved down, not up. Fundi normal. Difficulty with lips, preventing whistling. Voice nasal. Arms weak. Eighteen months later able to move left eye halfway to outer canthus and up one-sixth of an inch. Left eye moved out only when tested separately. Appeared to remain in same condition though away from observation till death four years after.

(2) Girl, æt. 29. At age of 26 general muscular feebleness appeared and gradually increased. Double ptosis, though lids were sometimes raised fully. Movement of eyes upward impossible, very limited down and out. Convergence limited. Reaction of pupils normal. Nasal smile. Lips weak. Voice nasal. Palate little raised in phonation. When patient was tired swallowing was difficult. Occasional nasal regurgitation. Muscles of mastication easily tired. Muscles of neck weak, letting head fall back or forward. Arms and legs feeble; could only walk two hundred to three hundred yards. Knee-jerk normal. No wasting. Slight improvement during next three years. March, 1902: Ocular symptoms much the same. No weakness in neck muscles. Generally stronger.

(3) Woman, æt. 39. At 29, amputation of cervix uteri for carcinoma. Subsequently two miscarriages. Seen first in June, 1895. Symptoms noticed last two years. Fixed aspect of eyes. Nasal smile. Could not whistle as formerly. Voice nasal. Palate raised very little in phonation. Slight occasional dysphagia. Contraction of masseters weak, especially right. Marked double ptosis. Left eye used in fixing. Slight divergence of globes increased on looking up. Upward movement half of normal. Movements of external recti half, internal recti quarter normal. Downward movement

good. Six weeks later right ptosis increased. Injections of strychnine. In one month better, though weaker again six months later. Variations in corone. Died in six months' time from influenza and bronchitis, the thoracic muscles being too weak to expel mucus.

4. Girl, æt. 14. First seen by Sir W. Gowers at the age of 12. Family, nervous. Onset of disease gradual at 8, ascribed to influenza. Tall, nervously sensitive, marked ptosis and consequent backward carriage of head. Frontales act well. Lower part of face much weaker on right than left. No nasal smile. Can whistle with effort. Voice nasal. Tongue normal. Upward movement of eyes defective, downward and lateral movements only fair. Convergence absent, though each internal rectus acts fairly with the opposite external rectus. Accommodation and vision good. Hands very weak, left hand much less excitable to single faradic shock than right. No attempt to obtain myasthenic reaction. Knee-jerk good at first, diminished on repetition, at tenth tap nearly disappears, recovering after a few seconds' rest. Muscles of left hand thinner than right. No definite local wasting. Has recently had two epileptiform attacks with minor attacks in intervals. Slight weakness of adductors of vocal cords. Masseters, right contracts less strongly than left. Walks and rides well.

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Auerbach.

32.—Woman, æt. 37. Immediately after severe shock at age of 20, great weakness of limbs and feeling of respiratory oppression. Diplopia next day, soon followed by partial ptosis, weakness of lips, tongue, face, and muscles of mastication and deglutition. Symptoms aggravated by attacks of influenza, menstruation, and strain, bodily or mental. Better in evening. Ocular movements slow. Phonation perfect. Fatigue present in muscles of tongue, face, eyelids, pharynx, jaws, five or six movements generally sufficient. Legs and arms weak, but show nothing characteristic. Myasthenic reaction present. Slight tendency to incontinence of urine and fæces. Knee-jerk exaggerated. Inhalations of oxygen caused dyspnoea.

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Jacoby.

34.—Girl, æt. 20, shown to New York Neurological Society. Quite well till May, 1901, when, while reading aloud, her voice was noticed to falter. This defect became more marked. Later diplopia, nasal speech, and nasal regurgitation of fluids. February, 1902, slight weakness of right hand. Mouth broad, lips thick, face expressionless. Difficulty in pouting lips. Inability to close eyes. Reflexes can be exhausted.

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Hingston and Stoddart.

35.—Contractor, æt. 70. When 63, neuralgic pains all over limbs and body, finally limited to left leg. Confined to bed for weeks. Urine then high specific gravity, with much sugar, which later was reduced to a trace. At age of 70, albuminuria set in, and steady loss of energy and strength. Relaxed diet seven weeks before death, from which time final illness appears to date. Gradual increase of general weakness. Became exhausted during dressing. Slight bilateral ptosis. Soon difficulty in swallowing, nasal regurgitation of fluids. Movements of limbs and trunk performed fairly,

but easily exhausted. No atrophy or loss of sensation. Electrical reactions not tried. Knee-jerk at first a little exaggerated, partly exhaustible. No clonus. Nystagmoid jerking on lateral deviation of eyes, increasing with prolongation of movement. No diplopia. Voice strong at first, reduced to aphonia after a few minutes. Loud aortic second sound. Bladder and rectum normal. June 29th, dysphagia increased till death, July 13th.

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Byschowsky, Z.

36.—On 11th August, 1899, consulted by Fraülein L.S., 19 years old. Three days ago, following, it is said, "a cold," dropping of both upper lids. Similar attack four years ago, but gradual, lasting three days and going upon one application of electricity. Since then well, except for headaches. Now has dull pain in eyes. Led into room because unable to guide herself. Complete bilateral paralytic ptosis. Eyeballs, generally turned down, can be turned in all directions after certain effort. Knee-jerk active. Speech a little nasal. While patient was under observation, involuntary momentary raising of eyelids. She felt better after weak galvanic current had been applied to eyes. Next morning ptosis had gone. No traces of hysteria. On 7th July, 1901, again unable to open eyes. "Nervous" for several days. Deep pain in eyes, while eyelids felt heavy. Headache. No vomiting. Walking and eating tires. Face apathetic, showing no paralysis. Application of electricity again successful. 12th July, 1901, violent headache. Weakness in arms. Marked myasthenic reaction in both. Arms at first raised well; after five or six times tire quickly. Similar phenomena in elbow and fist. While facial muscles were being examined with the constant current, patient suddenly cried out "schön!" (splendid), and after a few minutes opened both eyes, the ptosis disappearing. Myasthenic condition of upper limbs remained, with slight variations, unaltered till 31st August, 1902.

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Fajersztajn.

39.—Four cases, one of which came to post-mortem examination. No definite part played by infectious disease, neuropathic diathesis, or overwork. Three women, æt. 20, 27, and 30, and one man, in whom the first symptoms appeared at 62. All cases showed slow development, and became progressively worse by individual attacks divided by remissions, which were marked only in one case. No pain or disorder of sensation. All four showed ptosis and great muscular fatigue. In one case, general myasthenic reaction certain; in second, in biceps and interossei; third, in numerous muscles of extremities; fourth, in muscles supplied by facial and motor division of fifth. For post-mortem, see p. 79.

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Peterson.

40.—Woman, æt. 38. First seen, October, 1900. For several weeks difficulty in speech and some dysphagia; condition resembling, to some extent, bulbar paralysis. No history of syphilis or alcohol. Some weakening of one side of mouth. Slight deviation of tongue to right. Very peculiar speech, or dysarthria. No atrophy, and no actual paralysis. Gait, imitation of spastic, with no spasticity. Anæmic. Very weak. Pupils normal. Knee-jerk subtypical. Bore a normal child in March, 1901. Condition up to November, 1901, unchanged. Quick exhaustion in mastication, speech, swallowing, walking.



Mohr, L.

43.—A joiner, æt. 37. Typical case of Banti's disease, with primary swelling of spleen, large liver, icterus, anæmia, hæmorrhagic diathesis. About eight months before death rapid onset of diplopia, ptosis, weakness of muscles of swallowing and chewing, difficulty in articulation. Rapid fatigue of muscles, typical myasthenic reaction in quadriceps femoris, adductors, tibialis anticus, biceps brachii, masseter. Character of speech, bulbar. Complete failure of voice after speaking some time. No atrophy or disturbance of sensation. Disposition excitable. For post-mortem, *vide* p. 79.

Meyerstein, R.

44.—Seamstress, æt. 33, not overworked. Goitre for twenty years. Christmas, 1903, diplopia. April, 1904, back of neck stiff and head frequently fell forward. This improved, but after three weeks considerable weakness appeared in arms, which were very easily exhausted. Frequent drooping of eyelids. Symptoms less marked in morning. Subject to palpitation, fits of sweating. Blushes easily. October, 1904, considerable ptosis both eyes, especially left, worse on repeatedly opening and closing eyes. Exophthalmos both eyes. Stellwag's sign. Weakness in wrinkling forehead and closing eyelids. Lower half of face unaffected. Muscles of palate, lips, tongue, chewing free. A goitre, the size of one's fist, occupying mainly the right lobe. Slight tremor of hands on fatigue. Grasp poor. Arms fatigued. Walk good. Thighs weak. No atrophy or loss of reflexes. Knee-jerk sluggish, not fatigued. Myasthenic reaction both biceps muscles, left deltoid and supinator longus. Heart a little dilated. Inconstant systolic bruit at apex and base. Pulse 110–130. Blood normal. Fatal attack of dyspnoea and cyanosis. Death November 7th, 1904.

Fuchs, A.

45.—(1) Servant girl, æt. 20. January, 1902, noticed difficulty in speech after prolonged speaking or reading. In the summer temporary diplopia appeared, then quick fatigue in walking, then tiring of arms, difficulty of swallowing. All symptoms lessen after short rest and return on exercise of the organ concerned. No organic disease. No atrophy. Slight paresis of upper extremities when at rest. Weakness of muscles of trunk and pelvis. After repeatedly shutting and opening eyelids ptosis is seen, on right more than on left. After speaking long voice is nasal. No definite myasthenic reaction. Trace of albumen in urine. Frequent change in degree of symptoms.

(2) A later description appears in the Wiener klin. Wochenschrift, 1904, xvii. p. 1422. Wasting of interosseous spaces 3 and 4 (right < left) and presence of foot phenomenon ("Fuss-phänomen") are now noted as having appeared.

Kohn, R.

46.—J. F., æt. 27. Four months pregnant. Has had four children, and has felt very weak since birth of last in December, 1901. Dizziness after walking. When tired, nasal regurgitation of fluids. Nasal speech after talking some time. Diplopia after gazing long at an object. Occasional inability to close eyelids. Constant pain in forehead, often shooting to

occiput. Epileptiform fits twice, first before age of ten, and second six years ago. Brother epileptic. Left pupil somewhat wider than right, both reacting well to light and accommodation. Feeling of tiredness in eyes. Occasional slight nystagmoid movements after long gazing. June 24th, 1902, swallowing troubles gone. Unable to keep arms raised. Grip rapidly exhausted. Lower extremities, sensation, and reflexes normal. Pulse, 80—90: respiration, 22—28. At first, myasthenic reaction readily got on biceps. No reaction of degeneration. After five days in bed, myasthenic reaction not obtainable. June 29th, much better. Can close eyelids completely. Left hospital, did active housework, and had a normal confinement, followed in two days by sudden dyspnoea, syncope, and death.

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Wescott and Pusey.

47.—W. E. F., male, æt. 20. Diplopia. Left vision, six-ninths; right vision, six-sevenths. Esophoria 22°, and hyperphoria 8°. Given glasses. In a month, *i.e.*, on December 8th, 1899, free from blurring of vision. No esophoria, and hyperphoria 3°. Well till July 3rd, 1902, when diplopia and blurring recurred. August 6th, 1902, diplopia, left vision, six-fifths; right vision, six-fifths. September 26th, 1902, paralysis of convergence. Slight ptosis upper lid. Reaction to light and accommodation good. Works at desk comfortably with one eye closed.

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Moyer.

48.—Male, æt. 43. Diplopia, November 6th, 1899, which disappeared and recurred intermittently. Myopic. Later failure of convergence from paralysis of internal recti. Then limitation of movement of all eye muscles except external recti. Later, marked general weakness and stiffness of legs. Once or twice marked ptosis, more in left eye, lasting two to three hours, reflexes, superficial and deep, never in both sides at same time. Fundus oculi normal. Knee-jerk and all reflexes, superficial and deep, easily got. No atrophy. Numbness index finger. Face and jaw muscles weak. Voice said to have been always peculiar.

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Link, R.

49.—Male, æt. 43. April, 1901, twinges in eyes. Left ptosis. Diplopia. In June, heaviness in calves and thighs, then in axillæ, wrists, fingers. Involuntary rotatory movements ("Umdrehungen") of hands, which could not be stretched out. Eye symptoms varied in degree, being exaggerated by much movement. General weakness and readiness for fatigue. No atrophy. Mask-like face. After five or six attempts to whistle mouth cannot be shut. Nasal regurgitation, and difficulty in swallowing. Weakness of arms. Patient cannot raise himself in bed. Myasthenic reaction in right supinator longus and less in right deltoid. August 28th, sudden dyspnoea. Cyanosis. Pulse 100. Death in one and a-half hours. For account of post-mortem (Zellherden), see p. 79.

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Hey, J.

51.—(1) Bertha H., æt. 40. Wife of worker on railroad. Rickets (die englische Krankheit) as a child. Onset of illness in her thirty-second year, in October, 1891, following three hours' exposure to wind and rain. On

same day stiffness in feet hardly allowed her to climb the staircase. Pain in the right knee. After eight days she gave up work from general weakness, especially of arms and legs. Anæmic. Condition continued with slight variations till spring of 1894, when she became worse, and could only raise her arms once or twice. Soon tired in speaking. Much the same till Christmas, 1898. Extremities weaker, speech worse, often nasal. Swallowing often difficult. Constipation. Admitted into hospital 7th July, 1899. Nutrition fair. Slight goitre. Some ptosis bilateral, more on left. Movements of eyes to right and left incomplete, also upward movement, which is associated with nystagmoid jerkings. Lips weak, cannot whistle. Palate and tongue strong. Speech nasal after counting 50, indistinct at 66. Arms, legs and glutei weak. Gait at first normal, soon tottery. No atrophy or disturbance of sensation or reflexes. Myasthenic reaction in right biceps, thigh and leg muscles. Some apathy, symptoms worse on emotion, fright or anger. 8th September, 1899. Better, went home. Relapse in three weeks. Left side of face weaker. Condition much the same till 12th November, 1899.

(2) Pedlar's wife, 27. Nervous mother. Attributes onset of symptoms to fatigue of nursing sick child in summer of 1899. In autumn noticed her knees give way, and inability to do hair. After variations, worse in August, 1900. Better under treatment till relapse at Christmas. Could not go a step or rise from chair alone. Condition on 19th June, 1901. Development fair. After repeated movements, tiredness of eyes and diplopia. Pupils normal. Speech tires her, and sounds as if she had something in her mouth. Swallowing tires, and is difficult at end of meal. Occasional nasal regurgitation of fluids. Chewing muscles soon exhausted. Arms nearly normal. Cannot raise herself in bed without their help. Bladder and rectum free. Movements at hip weak and soon tired. Gait unsafe after a few minutes. No Romberg's sign or disturbance of sensation. Myasthenic reaction. Left biceps, extensors of forearm, quadriceps, right tib. anticus. 25th June, frequent variation of space between eyelids. Fixed facial expression. 29th June, depression. Frequent crying. 4th July, often worse in morning than at midday, worse again at night. 29th July, becoming worse. Sent home at request of relations. Frequent morning vomiting. No question of pregnancy.

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Steinert, H.

52.—Man, æt. 20. August, 1902, syphilis with rash. January, 1903, pains in the legs lasting a month and weakness of whole body. Took to bed. Cramps over whole body. Condition on March 18th, 1903. Very thin and very dry skin. Much wasting. Hair very thin. Healed bed-sore on sacrum. Scoliosis. General weakness. Muscles left leg somewhat weaker than right. Glutei very weak. Lordosis of lumbar vertebræ. To raise himself from prone position has to use hands. Difficulty in raising arms. "Winged" shoulder blades. Gait laborious and stiff. Knees pressed out and feet fall flat. Movements of limbs perfect at first, fail after a few repetitions. Activity recovered after short rest. Breathing exhausted by a few forced respirations. By using alternate groups of muscles and sparing effort, can walk an hour, though if he stood on one leg he fell over after a few seconds. Definite myasthenic reaction. No reaction of degeneration. No atrophy. Polyuria, 3-4½ litres in twenty-four hours. Taste of sweet lost left half of

tongue. Deep reflexes difficult to obtain on admission (March 18th). On April 17th, right knee-jerk active, left still sluggish. Achilles jerk, right brisk, left absent. All reflexes soon exhausted. Romberg's sign. Symptoms worse towards evening. April 20th, extraction of teeth; 24th, conjugate movements of eyes fail after a few repeated movements, also convergence and accommodation. Reaction of pupils normal. Facial muscles and orbiculares palpebrarum fatigued. Chewing soon tired. Neck muscles letting chin drop forward for just a minute on chest. After a few lateral movements of eye, upward movements also fail. Sense of passive movements of ankles frequently wrong. 8th August, left hospital. No weakness, fatigue, or myasthenic reaction or polyuria. Reflexes normal. Gain in weight.

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Diller.

53.—Female, æt. 29, married twelve years. Has had three children. No miscarriages. Diphtheria as a child. Chronic alcoholism. Two years ago spent five months in bed with general muscular weakness, since which she has always been tired. July 11th, 1902, caught cold. Sudden difficulty in speech, which became almost unintelligible. Several days diplopia. Admitted into St. Francis' Hospital with pyrexia (Temp. 103·8° F.). Temperature, high for fifteen days, fell by lysis. On July 31st rose to 103° and large circumscribed areas of œdema ("angeio-neurotic") appeared on right shoulder, arm, hip, leg. Very painful. No redness. Disappeared in five days. Aug. 7th, face mask-like, muscles weak. Speech slurring in character, becoming more so as she talked. Daily variation. No ocular palsies. No atrophy. Knee and Achilles jerk and skin reflexes sluggish. Blood, red corpuscles 4,226,000 per cub. mm. Urine upon admission contained albumen and granular casts, afterwards absent. September 23rd, general improvement.

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Myers, C. S.

54.—Eliz. D., æt. 22, confectionery packer. Christmas, 1898, eyes became weak, and were not benefited by glasses. Good Friday, 1899, sudden dysphagia and nasal regurgitation, which has since occurred occasionally. Some difficulty in closing jaws. Occasional loss of power in arms, especially in extensors. In July, ptosis, first of left eyelid, recovering later and appearing in right side. Admitted under Dr. Gee, in St. Bartholomew's Hospital, August 10th, 1899. Nervous-looking girl. Mouth open. Movements of right eye limited in all directions, of left eye especially up and down. Upward squint of left eye. Face muscles good. Had to support lower jaw in eating. Palate feeble. Tongue and limbs normal. Speech thick. All muscles reacted well to faradism, and seemed improved. Daily variation of ocular paresis. August 20th, to prevent her supporting jaw with hands, they were put into splints. As she was being fed with milk in a spoon, a fatal choking attack occurred. For post-mortem see p. 79.

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Berger, A.

55.—Anæmic girl, æt. 17. Shown before the Gesellschaft f. inn. Med. in Wien. Slight right ptosis and facial expression stiff. Lips pouted with difficulty. Whistling impossible. Vocal cords normal. Soft palate not raised. At beginning of sentence speech quite normal, becoming nasal after

four or five words, unintelligible after ten or twelve, but intelligible again after a few seconds' rest. No weakness or abnormal fatigue of muscles of trunk or extremities. No myasthenic reaction.

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Hoffmann, A.

56.—Postman, æt. 32. In 1899 had paralysis of right eyelid. In 1901 quickly-increasing weakness of arms, legs, eyelids, muscles of speech and swallowing. Right side worse than left. Swallowing became almost impossible. Patient could only speak a few words. Tongue put out with difficulty. Could not hold head upright. Walking impossible for weeks together. Arms could not be raised to horizontal. Improvement. On 31st January, 1904, patient had been fully capable of work for a year, only trace of disease being weakness of right levator palpebrarum superioris, letting lid hang powerless after opening or shutting eye ten or twelve times. Treatment, strychnine and galvanisation.

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Oppenheim, H.

57.—Woman, æt. 48. Employed in domestic agency. Attended first on August 20th, 1897. Six years shortness of breath, palpitation, tremors of hand. Diplopia for a few weeks in 1896. Now loss of sleep and appetite, irregularity of bowels, polyuria, and hyperidrosis. Pulse very rapid. Tremor of hands much increased by active movements. Tendon reflexes exaggerated. Diagnosed as hysteria, or morbus Basedowii. In October, 1897, for the month past, difficulty in speaking and swallowing, slight ptosis and lagophthalmos. Speech nasal after talking. Palate moved well. Pulse 90–96. Arms strong. No myasthenic reaction. Myasthenic reaction later in extensors of fingers (middle and end phalanges of second and third fingers could not be completely extended). November 28th, 1898, great weakness. Could neither whistle nor blow out a light. Soft palate and diaphragm feeble. Respiration slow and shallow. March 23rd, 1899, attack of severe dyspnœa for two hours. Marked ptosis, with nearly complete paralysis of orbiculares palpebrarum and oris. March 26th, exhaustion and cachexia. Dyspnœa, paralysis of muscles of swallowing and diaphragm. Death. For post-mortem, see p. 78.

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De Léon.

58.—Woman, æt. 35, unmarried. One sister has exophthalmic goitre, another Bell's palsy, while a brother committed suicide. From age of fourteen attacks of right-sided migraine, with vomiting. When 22, morning after an attack of pain in right frontal region, slight drooping of left eyelid, while at times she saw double. Treated with galvanism. Trouble went in six days, recurring at intervals, more often in left than right. In 1899, headaches less frequent, but generally followed by eye symptoms, incomplete left ptosis, inability to move left eye up. Limited lateral movements both eyes, especially left. Pupils normal. Weakness of mastication and lower limbs. Better in morning. 1900, paresis worse in right eye. Ptosis symmetrical, over-action of frontales and arching of eyebrows. External recti and obliqui affected, only downward movements free. Weakness of shoulders better after rest, worse after treatment by massage and baths. 1903, frequent rests during eating, "dysmassesia" and fatigue after swallowing. Orbiculares palpebrarum both weak. She cannot whistle.

"Hutchinson's" facies, expressionless. Tongue cannot hollow itself. Occasional nasal regurgitation. Nasal voice. Neck muscles free. Cannot raise arms. Walking very difficult. No diminution in volume of muscles. No reaction of degeneration. Myasthenic reaction in both deltoids. Contraction disappears in less than two minutes to tetanic stimuli. Occasional attacks of dyspnoea. Always worse during menstruation.

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Pel.

59.—Milliner, æt. 22. Worked fifteen hours a day. Seen first on May 15th, 1904. Complained of difficulty in speech, swallowing, and general weakness. Onset in June, 1903, with fatigue of speech, and later of chewing. Eyelids heavy. January, 1904, diplopia. Deep respirations impossible. Two suffocating attacks. Speech became nasal. Nasal regurgitation. Lips and tongue stiff, and latter scarcely movable. Better when cheerful, worse when depressed. In May, soft palate sluggish. Tongue wrinkled and atrophied. Frontales, orbiculares palpebrarum, levatores labii weak and easily tired. Weakness of upper and lower limbs. Myasthenic reaction in tongue, which became less atrophied. Much fluctuation. July 3rd, rigor. Pains in back. Vomiting. Temperature 40° C. Lividity. Rapid respiration. Mucus in throat. Death in three hours. For autopsy, performed by Sitsen, see list of post-mortems, No. 109. It was later learnt an elder brother was also overworked and subsequently paralysed, recovering after one and a-half years' rest. A second brother became neurotic after overwork, and "finally a vegetarian."

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Sachs, B.

60.—Man, æt. 35. When 16, had chorea, lasting some four months. April, 1902, tongue for six weeks felt very heavy, which recurred September, 1903. Afterwards at times lost use of tongue. Became very nervous. December, thick bulbar speech. Head inclined forward and to right. Hands weak and tired after slight exertion. Knee-jerk absent. March, 1904, speech and general condition better. Vision occasionally limited. Unable to look up well. Knee-jerk now normal. Occasional choking feeling on swallowing, and occasional regurgitation. Mercurial salivation. No electrical alterations or atrophy. Slight twitching of mouth. (Case somewhat doubtful, A. P.)

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Pierce Clark.

61.—Shown before New York Neurological Society.—Woman. Rapid exhaustibility of muscles, especially of left side, including shoulder and pelvis. Some persistent paresis. Symptoms very variable. Some ptosis. Expression sleepy. Has been bedridden three months, and steadily worse up to three weeks ago, when she was given thyroid, and great improvement ensued two days later. She took thymus extract also for a short period. "Gluteal walk." Suffers from "dead fingers." Two months ago facial œdema (most marked in lips), which slowly passed away. Atrophy of tongue. Periodic attacks of diarrhoea. Nasal voice. Myasthenic reaction, especially in deltoids and rapezius. "Spells of dropping" in the streets. Formerly some difficulty in swallowing.

Warrington, W. B.

62.—C. M., married woman, æt. 25. Admitted to hospital February 25th, 1904. Progressive weakness in limbs first noticeable eighteen months ago, during first months of pregnancy, rapidly progressing and very marked when child was born. Thickness and difficulty in speech. Trouble in swallowing, with occasional nasal regurgitation. Well nourished. Fixed expression. Lips constantly apart. Neck bent slightly back. Some ptosis. Swallowing painful and spasmodic. Gait slow, rather waddling. Can only walk ten yards. Cannot rise from bed or lift one knee over the other. Weakness chiefly in ileo-psoas and glutei. Movements of leg and foot fair. No wasting. Knee-jerk brisk and not tired. Grasp very feeble, soon fails. Cannot raise arm to right angle. No myasthenic reaction. Trunk muscles weak. The intercostals and diaphragm act well. Cannot close lips or distend cheeks. Nasal smile. Ptosis. Levatores palpebrarum and frontales soon tire. Lateral movements deficient, upward very poor, downward less so. Mastication weak. Palate sluggish, not exhausted by phonation. Partial reaction of degeneration in face muscles. Three months later, myasthenic reaction in deltoid and biceps. Condition much the same. (For Cæsarian section see No. 78.)

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Von Michel.

63.—Two cases shown before the Berliner Ophthalm. Gesellschaft, June 16th, 1904. Both purely ocular.

(1) Man, æt. 47. The recti interni chiefly affected; at times the recti superiores.

(2) Child of 5. Myasthenic reaction of orbiculares. Ptosis increased by action of gazing about. Intraocular muscles not affected. (Inadequate account. A.P.)

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Bielschowsky, A.

64.—Clara K., æt. 17. In February, 1904, ptosis, first right, then left eyelid, recurring after temporary improvement. Diplopia absent when seen on July 4th. Girl stupid and frightened. Never ill before. History of globus hystericus. Closing of lids weak. Attempts to move eyes laterally results only in slight quiverings. Raising of eyes impossible, lowering possible in small degree. Crossed diplopia for near objects. Pupils equal, react to light and accommodation. Speech nasal and thick. Put on galvanism and mercury inunction. In seven weeks left ptosis less, right more. Amenorrhœa. 2nd September, 1904, weakness lower limbs, dragging of feet. Difficulty of swallowing, nasal regurgitation. Chewing toilsome and painful. Speech fairly clear in morning. Arms weak and, like legs, worse in evening. Improved in bed. Myasthenic reaction in lip muscles. "Bell's Phenomenon," i.e., as shutting of lids gets weaker, eyes move upward.

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Lawford, J. B.

65.—Baker, æt. 51, married. Good health till fourteen years ago, when during influenza he noticed drooping of lids. This gradually progressed, increasing quicker in subsequent attacks of influenza. He worked long hours in bakehouse. Ten years ago had some weakness of limbs. Legs worse after rheumatism eight years ago. Worked till last Christmas,

when he kept his bed with influenza for thirteen weeks, which left increase of ptosis and weakness. Admitted into Moorfields, April 13th, 1904. Tired, vacant look, with obliteration of facial and frontal furrows. Ptosis constant, and almost complete, especially left. All ocular movements very slight. No diplopia. Occipito-frontales very weak. Pupils normal. Some myopia. Visual fields normal when lids are raised, which is easily done by finger. Temporals and masseters weak. Tongue weak, protruded straight. Cannot whistle loud. Paresis soft palate. Nasal regurgitation. Speech nasal. Abductors of vocal cords very weak, adductors good. To see better raises head, but cannot do so long. To raise upper lid, wears spectacle frame with wire crutches fitted to upper part of eye-pieces. Grasp weak, muscles of lower limbs, abdomen, erector spinæ, trapezius weak. Muscular co-ordination and sense good. Respiration shallow. No trouble with bladder or rectum. Conjunctival reflex very dull. Knee-jerk less marked when frequently elicited. (Notes by Mr. W. Anderson.)

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Taylor, J.

66.—Painter, æt. 46. Has had lead colic and "painter's gout." No definite history of paralysis. Ptosis ten years ago, recurring intermittently next six years, while last four years it has been permanent. Diplopia nine years ago. Cannot see to read for long at a time. Upper and lower extremities weak and easily exhausted. Now ptosis (right > left), external ophthalmoplegia. Pupils react to light. Mastication difficult. Articulation good. Myasthenic reaction in affected muscles, especially flexors and extensors of wrists and fingers. Reflexes and sphincters normal. Difficulty in breathing not relieved by tracheotomy. Death. Nothing found post-mortem. (See list of post-mortems, p. 80).

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Rennie, M.

67.—(1.) Youth, æt. 19. Seen in February, 1903. Has been ill eighteen months. Heavy cigarette smoker. No history of alcohol or lues. Onset with difficulty in swallowing food, increasing up to time of admission. Occasional nasal regurgitation. After nine months eyelids drooped, in two months nasal voice; fatigue. He fell after running twenty yards. Condition in February, 1903: Pulse 56-68. Well nourished. Speech in morning good; after talking a short time, nasal. Movement of eyeballs limited, especially outward. Marked ptosis right and partly left; occasional slight diplopia. Face expressionless. Nasal smile. Soft palate does not contract on phonation. Cannot whistle. Muscles of trunk and limb fairly strong. Reflexes not exhausted. Myasthenic reaction in leg muscles. After six weeks' rest, good food, and cod liver oil, much improvement, disappearance of ophthalmoplegia and dysphagia.

(2) C. T. C., Farmer, æt. 27. Steady man. Jockey; had taken thyroid last two years to reduce weight. In December, 1902, drooping of eyelids. Following fall from horse he rapidly became weak. Attacks of difficulty of breathing and swallowing, and cyanosis. Weakness legs and arms. Condition on admission to hospital, February, 1903, lying in bed on back, unable to raise himself or easily turn over. Nutrition fair. Movements of eyeballs limited in all directions. Marked diplopia. Ptosis both eyelids (left > right).



He could close eyes completely, but not resist their being opened. Over-exertion of occipito-frontalis to overcome ptosis. Face expressionless, all facial movements being restricted. Cannot whistle. Swallows fluids only with difficulty and when sitting up. Mucus accumulates in throat. Voice nasal and occasionally unintelligible, especially after speaking. No palate reflex. Neck muscles weak. Head dropped. Grasp feeble. All reflexes active. Myasthenic reaction arms and legs. Fed with nutrient enemata. Fatal attack of dyspnoea three weeks from admission.

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Colman (Shown before Neurological Society, October 27th, 1904).

68.—L. M., æt. 23, Female. Rheumatism twice. Slight systolic murmur. No history of diphtheria. Nine months ago noticed tiredness of lips and tongue when talking. Voice became husky. Arms and legs easily tired, recovering after short rest. Condition on October, 1904: Well nourished. Constant weakness of levator palpebrae superioris and orbicularis oris. Lower lip pendulous. Voice "muffled" and nasal. All muscles easily tired. After reading aloud palate almost immobile. At end of meal food nearly escapes between lips, and nasal regurgitation. Symptoms soon pass off. Aching in fatigued muscles. Tingling in lips, palate, limbs. No anaesthesia. Reaction to isolated faradic stimuli lost in two minutes, lasting longer for tetanization.

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Hun.

69.—H. K., æt. 32, Engineer. Antecedents good. Admitted October 8th, 1900. Onset nine months before when in perfect health of gradual left ptosis, worse towards evening, followed by weakness in neck muscles, quick fatigue of left hand, forearm, and right middle finger. Lips weak, and whistle with difficulty. Six months later weakness of left leg with pain in calf. Past three months double ptosis (left > right), difficulty in mastication, hoarseness after talking (voice never nasal), weakness of hands and legs. After walking two hundred feet general exhaustion, quick respiration, palpitation and muscular tremor. Legs give way and he cannot rise. This muscular weakness comes on after continued use of any group of muscles. No paræsthesia. Muscular development good. Knee-jerk lively. No ankle clonus. Hæmoglobin 78½, red corpuscles 5,940,000, white 7,300. Smear normal. Daily variation. Myasthenic reaction deltoid, biceps, and median nerve. December 9th, 1900, worse. Zygomatic weak, especially right. When laughing does not raise upper lip. Nasal voice. Neck muscles do not support head. Temperature 97-98°, Pulse circ. 80. Seems to do best on galvanism and hypodermic injections of strychnine. May 16th, 1901, worse. Thyroid useless. November 14th, death after frequent paroxysms of suffocation. See list p. 79.

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Brissaud and Bauer.

70.—Domestic, æt. 46. Born in the Haute Loire, a goitre district. Thyroid swelling noticed when 20. Married at 25, has one child. Has never been strong. Two years ago for several months darting pains in limbs, especially in muscular masses. Very fatigued and gave up work. At end of May worse. Vomiting every day immediately after meals. Now bedridden. Vomiting and condition so bad that she entered the Hôtel Dieu. Lumbar

puncture showed absence of formed elements in fluid. Vomiting stopped. Great emaciation. Absolute incapacity for movement. Exophthalmos. Knee-jerk got with difficulty. Left pupil smaller than right. Lumbar puncture repeated. Fluid normal (helping to exclude tabes). General state improved rapidly. Splendid appetite. Soon could sit up. At end of September could take a few steps. Hyperidrosis. Urine normal. Noticeable variations. Diminution in force and atrophy of all muscular masses. Electrical reactions normal. Forced lateral movements of eyes produce nystagmoid movements. No ophthalmoplegia externa or true ptosis. Occasional heaviness of pupils. Slight trouble of speech during attacks of vomiting.

Sterling, W. L.

71.—(1) A. K., æt. 45, labourer's wife. Disturbance in speech in summer, 1901. Diplopia since beginning of April, 1902. Nasal voice. In middle of April, difficulty in chewing and swallowing solids, which caused suffocating attacks. Nasal regurgitation of fluids. Feeling of dryness in throat. Difficulty of speech came on with fatigue and emotion. Arms fail after long work. Fingers often "go to sleep." Formication. Cannot hold her water long. Some weakness in opening and closing lids. Three healthy children. No abortion. Condition 5th July, 1902: Pupils normal. Drooping right upper eyelid and weakness of raising both. Slight paralysis right abducens. No exophthalmos. Diplopia on looking to right. Face muscles slow in expression. Drooping of corners of mouth, very noticeable in laughing. Tongue normal. Dyspnoea and cyanosis after forced respiration. Voice weak and nasal after reading. Soft palate feebly raised and motionless after repeated intonation. Similar failure in palatal reflex. Upper and lower limbs not strong, but no pathological weakness. Deep reflexes exaggerated. Slight deadening of touch sense in fingers. Myasthenic reaction left supinator longus. After improvement, relapse on 25th July, 1902, following death of husband. Myasthenic reaction in left sterno mastoid and extrinsic laryngeal muscles.

✓ (2) Boy, æt. 15. "Schlosser-geselle," sent from ophthalmic clinique, where tubercles of the choroid had been detected. Gradual development of disease in last ten weeks with daily variation. First symptom, heaviness of lids, hands and neck muscles readily tired. Fatigue in walking and climbing stairs. Not overworked. Eyelids easily opened in morning. Condition: Well built. Expression sorrowful. Paralysis right levator palpebræ superioris and inferior rectus. Pupils normal. Weakness orbiculares oculi, especially right. Drooping right corner of mouth, and smoothing right naso-labial fold. Weakness in closing mouth. He cannot hold a cigarette long. Good myasthenic reaction both sides of face, not in extremities. Knee-jerk normal. December 20th, 1902, worse. Difficulty in swallowing. February 13th, 1903, expression far more sorrowful. Nasal regurgitation of fluids. Weakness in arms; less in forearm and hand. Walking soon tires. Fibrillary contractions of tongue, which can only be protruded eight to ten times. Wrinkling of forehead, and whistling now impossible. Knee-jerk weak and exhaustible. February 19th, 1903, death with dyspnoea and complete paralysis of muscles of swallowing and speech.

(3.) A. N., æt. 25, woman; sent on from eye clinique with right ptosis. History of frequent diplopia last six months. Paralysis of right levator

palpebræ superioris, and rectus externus. Right ptosis had occurred two years before, and again in previous year. Much variation. Better in morning. No fatigue elsewhere. Has had one child, no abortions. Condition when seen: Weakly and with miserable expression. Right eye tremulous after extreme excursions. Pupils, knee and Achillis jerk normal. Myasthenic reaction and readiness for fatigue in left deltoid. March 20th, 1902, worse since start of menstruation yesterday. Respiration 36 per minute, harassed, and needing accessory muscles. Right rectus superior, and both orbiculares oculi fatigued. Myasthenic reaction in left orbicularis oculi. Some dulness over sternum. June 2nd, 1902, better. Abduction of right arm affected. February 5th, 1903, generally better. Occasional headaches.

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Raymond.

72.—Grocer, æt. 21. July 14th, 1903, sudden inability to articulate. Cold sweats. Both phenomena went away in five minutes. Dysarthria reappeared September 15th, and by middle of October these crises of lingual paresis came on whenever he wanted to talk. Some weakness of upper limbs. Starting work at six, by eight o'clock he could not close his hands. Worse after cold, better with heat and rest. Diplopia came on, March, 1904. Condition, April, 1904.—Voice nasal tone, which is said to have followed blow on nose at age of fourteen. Much more marked after talking there minutes, while speech became confused. Deglutition and mastication quickly exhausted. Lean in figure, face expressionless. Lagophthalmos, mouth constantly part open, lips turned out. Cannot whistle. Flexion of neck nearly normal, extension and lateral inclination very weak. Upper limbs, simple weakness, especially of hands, fingers, and all shoulder muscles. Reflexes and sensation normal. Frequent noises in ears. Poor excitability to galvanism and faradism in orbicularis oris. Lumbar puncture, March 16th, showed scattered lymphocytosis. No albumen. April 29th, myasthenic reaction in face muscles; less marked in upper limbs. Symptoms worse after injections of adrenalin; spermine injections were followed by slight improvement. Strychnine and caffein injections, and Tr. Iodi. had no effect. June, pulmonary congestion, "influenzal," with dyspnœa. Tachycardia. Absolute dysphagia. Death on 28th. *Vide* list of post-mortems, No. 27, p. 79.

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Burr, C. W.

73.—Brakesman, æt. 30. Malaria in 1894. Has had gonorrhœa, not syphilis. Seen October 14th, 1904. Much headache for two months. October 1st, right eyelid began to droop, especially in evening; jaw muscles weak, soon shoulders and arms, causing trouble in shaving. Muscular appearance. Walked well. Could not raise arms above shoulders. Arms and hands soon tired. Knee-jerk slightly more marked left. Pupils normal. Speech slow, voice weak, soon tired. Could swallow well if upright; if he leaned forward found solids stick in his throat. Daily variation, while he steadily got worse. November 20th, could hardly get out of bed or walk, and only hold his head up for a few minutes. Use of one group of muscles seemed to produce some weakness in others. Knee-jerk variable, occasionally not responding till after several taps. Marked ptosis (right and left). He could open eyes wide, but could not keep them so. Some tremor of tongue on extension. Face mask-like. November 23rd, 1904, sense of

suffocation lasting till November 27th, when he died, conscious to the last. Eyes: fundus normal, varying amount of contraction of visual fields, partial reversal of red and blue fields, and, later, colour confusion. Some weakness of some of external ocular muscles. See list of post-mortems.

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Spiller, W. C.

74.—Man, æt. 33. Ten years' headache, relieved about June, 1904, by treating the hypertrophic rhinitis. April 26th, 1904, everything looked crooked to both eyes; perfectly normal when one was closed. Vision good. November 14th, internal rectus right eye paralysed. Some ptosis left eye, soon of right. January 10th, 1905, when he takes off his glasses, upper lids begin almost at once to droop, and continue till eyes are covered. Wears cover over eyes alternately. Both upper lids fall when he looks down. Cannot look up or down well with right, or keep both eyes open at same time for more than a minute. Pupils normal. January 24th, 1905, cannot open eyes so well when he gets up as later, and can open them better in evening when lying down. Diplopia in looking directly forward, occasionally absent for a few minutes. Left sternomastoid somewhat exhaustible.

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Dodd, H. W., and Woodwark, H. S.

75. — Copying clerk, æt. 25. Admitted into Royal Free Hospital, November 10th, 1905. Quite healthy up to six weeks ago. Influenza at beginning of October, lasting for a week, though he kept at work. Afterwards he felt weak. Four weeks ago rapid tiring of jaw muscles after a few mouthfuls, and weakness of right leg. A few days later drooping of head when tired, aching of shoulders, and difficulty in holding himself erect, Walking tired quickly. Last two weeks ptosis, first right, then left, being hardly able towards evening to keep eyelids open. Nasal regurgitation. Weak hands. Occasional falls. Face listless, mask-like. Prominent lower jaw and superciliary ridges. In bed sat up with difficulty. In reading aloud first eyes tired and eyelids drooped, then jaw tired and had to be supported, and finally hands let book fall. Myasthenic reaction general, most marked in weakest muscles. Knee-jerk exaggerated, decreasing after several jerks. Occasional ankle clonus. Vision and visual fields normal. Occasional diplopia. Ocular movements incomplete, best downward. Occipito-frontalis normal. Cannot whistle or show teeth. Nasal smile. Pulse 80. April 11th, 1905, a little better.

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Frank, M.

76.—E. M., girl, æt. 10. Bohemian. Seen first in November, 1902, with double ptosis, right and left. Paresis of all extrinsic muscles of both eyes. Divergent strabismus right eye. Pupils normal. Mixed astigmatism. In 1900, drooping right eyelid, and few weeks later left. Defective movement of external eye muscles, except left externus rectus. No other abnormality. Ptosis absent in morning, comes on later. Eyelids can be closed, but not tightly. Occipito-frontalis weak, so to overcome ptosis head is thrown back. Gradually progressive limitation of movements of eyeballs till they are fixed in primary position. Lids, when raised three or four times, become completely exhausted. Slight myasthenic reaction occasionally found. No history of syphilis.

Dupré, E.

77.—L., woman, æt. 32. Admitted to Hospital, August 24th, 1901. Mother now dead, had Parkinson's disease. Convulsions in infancy. Had a child twenty-two months ago. Deserted by husband one month before accouchement, from which dates weakness of hands and lower limbs. Slight albuminuria during pregnancy. Twelve months after confinement eclamptic fit, which left her much weaker. Suckled her child and kept up to work as sempstress till present time, when too ill to work. Condition on admission: General weakness of arms, legs, trunk, insomnia. February, 1902, a little better. Face pale, listless. Nutrition and sleep good. Several nervous crises at onset of menstruation. Cannot get up when she lies down. No actual paralysis. General symmetrical hypotonia. Knee-jerk slightly exaggerated. No myasthenic reaction. Tongue affected. Speech quickly tires, also bite. October, 1902, sudden dyspnoea and small pulse. Death in forty-eight hours. Syncope. See list of P.M.'s.

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Gemmell, J. E.

78.—Sent on by Dr. Warrington (*vide* 62). Found to be pregnant. With advance of pregnancy much worse, the most trivial act causing the greatest exhaustion and dyspnoea. Sent on to Lying-in Hospital, October 12th, 1904, confinement being expected about October 20th. Condition grave, four attacks of dyspnoea in twenty-four hours. No sleep. Cyanosis. October 18th, the respiratory movements represented merely by hiccough. Patient was anaesthetised and subjected to Cæsarian section, which took forty-five minutes. No difficulties. Child, a well-nourished healthy girl. Recovery steady with improvement of respiration and gradual improvement of myasthenia. Still helpless when she left hospital. Slight improvement some weeks after. No dyspnoea. Sections of uterine muscle and rectus abdominis negative.

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Indemans, J. W.

79.—Mrs. N., æt. 28. Family history of nervous disease, hysteria, tabes. Before her marriage intermittent convergent strabismus, treated as hysterical. Went safely through two pregnancies. In her third, had a sudden excess of general tiredness and recurrence of strabismus. Better after rest. On April 21st, had a twenty weeks' old abortion. Recovery good, but more frequent onset of strabismus. Could not hold her arms horizontal. July 4th, speech slightly nasal; rapid tiring arms and legs, recovery after rest. July 28th, speech unintelligible. Intermittent ptosis. Flattening of nasolabial folds. Lips and ocular movements weak, especially rectus externus. Slight nystagmus. November, caught cold; nearly died from dyspnoea. January 10th, condition much the same. Chewing incomplete. Dysphagia. Paralysis of soft palate. Some bronchitis. April 26th, better, taking thymus tablets, two a day. May 31st, condition variable. Pulse, bladder, rectum normal. No atrophy.

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Launois.

80.—Robert, æt. 26. Press employée. Twelve hours a day. History good; none of syphilis. January, 1904, great depression owing to family bereavement. March, weakness right little finger. Tingling in fingers. Bilateral ptosis, left and right, with inability to open eyes (latter temporary,

former permanent). Vision has deteriorated last few years. Next, both hands affected, and could not button shirt. Astereognosis. He could not recognise objects in his pocket. Fingers feel stiff and numb in movement, not at rest. Some pain in joints. Formication of extremities gradually replaced by relative anaesthesia. July, 1904, weakness thighs and feet. In descending stairs walk uncertain, he has to hold balusters. Walks with little steps. Cannot control feet. Flatulent dyspepsia. August, slight headaches at evening. Type somewhat infantile. Left testicle undescended, and hair undeveloped. No Romberg's sign. Walks with broad base. Rapid exhaustion. Movements of upper limbs stiff, with no ataxy. Writing tremulous. Head droops forward. Difficulty in rising from seat. Can whistle at first, but soon fails. No myasthenic reaction or reaction of degeneration. Deep reflexes lost. Plantar reflex normal. Cremasteric and abdominal sluggish. Anaesthesia right fingers, first, second, third, fifth, and hypothenar eminence. Slight anaesthesia of tip of shoulder and cheeks. No nystagmus. Intermittent diplopia. Pupil reflexes normal. Cannot read at more than 50 cm. Right side of chest less developed than left. Sphincters normal, face dull, mouth open, laughing poor. Slight fibrillary tremors of tongue. January 15th, 1905, general condition better. More patches of anaesthesia. January 20th, lumbar puncture. Slight lymphocytosis.

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Buzzard, E. F.

82.—(1.) A. J., male, æt. 41. Admitted National Hospital, November 3rd, 1903. In 1892, injured left eye, and had muscular diplopia. Three or four years before admission patient had to lift upper lids when reading any length of time. March, 1902, heaviness of right leg, which soon tired. April, aching, first right foot, then left shoulder; later, all over body, coming on two hours after rising. Could not walk over fifty yards at a stretch. Dysphagia, salivation. Dyspnoea, and dysphasia rapidly set in after short talk. Loss of two stone since previous year. Condition on admission: movements feeble. Forehead wrinkled to counteract ptosis. Ocular movements very limited in range. No diplopia or nystagmus. Jaw movements fair. Forty-five faradic stimuli wore out left masseter. All facial movements weak, especially those of orbiculares palpebrarum and oris. Palate flaccid. Head could not be raised from pillow. Muscles of arm and fingers weak, shoulder muscles more so. Patient could not sit up by himself. Kyphosis. Shallow respiration. Muscles of lower limb better than upper. Aching, especially after movement. Diminished sensation over ulnar aspects of arms. Jaw-jerk present. Knee-jerk not tired by 300 stimuli. January, 1904, shooting pains lower limbs. Two attacks of respiratory failure. Knee-jerk now tired by six to twelve taps. Respiration chiefly diaphragmatic. Attacks of dyspnoea. Considerable relative anaesthesia and analgesia upper part of chest, ulnar side of arms, and hands and feet. Sphincters free. April 1st, much worse. Pains more severe. Analgesia more extensive. Nearly whole of arms anaesthetic. Death from respiratory failure, April 26th, 1904.

(2) Russian Pole, female, æt. 28. Admitted to National Hospital on October 8th, 1902, under Dr. Ormerod. Previous health good. Seven months ago pain in shoulders, arms, legs, and "pins and needles" in finger tips. Pains intermittent, worse in wet weather. Weakness arms and legs. One

month later sudden difficulty in talking. Diplopia, some dysphagia. Lately food tends to come back through lips. Condition on admission: Double ptosis, pendulous lower lip. Sweating skin. All facial muscles weak, especially orbicularis oris. Ocular muscles, first brisk, soon tire, also jaw movements and articulation. Tongue flabby. Limbs show deficient muscular power, especially after exertion. Sensation of pain—1, general aching and stiffness, especially after exertion; 2, sharp intermittent pains. A small patch of relative anæsthesia and analgesia over left shoulder. All reflexes brisk. Sphincters free. Myasthenic reaction. Left facial muscles exhausted in ninety seconds. December 10th, slight general improvement. Paresis of right externus rectus and consequent diplopia. January 20th, great pain in left leg, which is weaker. Gradually weaker. Can only swallow fluids. Sharp pains in face and neck. Dyspnoea when lying down. Knee-jerk easily exhausted. Fatal dyspnoea, November 6th.

(3) N. S., foreman, æt. 37. Admitted into London Hospital, under Dr. Head, February 3rd, 1904. Good health till "pneumonia," September, 1902. October, 1903, headache and vague pains. Stiffness of eyelids. Then diplopia, right ptosis, difficulty in articulation. Improvement till a week after Christmas, when articulation more difficult, jaw dropped and head tended to fall forward. Dysphagia at end of January. February 3rd, 1904, varying bilateral ptosis. Lower jaw dropping, and has to be supported for speech. Complete external ophthalmoplegia. Pupils normal. Face expressionless. Palate feeble. Voice weak and whispering. Tongue tired when protruded twelve times. Myasthenic reaction in sterno-mastoids. No sensory disturbance. Knee-jerk brisk. March 18th, weaker. Two choking fits. April 15th, speech nasal. Blood-count normal. September 23rd, dyspnoea. Death.

(4) H. B., schoolmaster, æt. 40. Admitted October, 1899, under Dr. J. Buzzard. Uncle died in an asylum; aunt had "creeping paralysis." Healthy till Christmas, 1892, when little and ring fingers felt temporarily weak. In 1893, occasional diplopia, recurring in 1894, when voice after a few minutes became nasal. Right ptosis. In 1897, weakness of lips, tongue and thigh. July, 1898, palpitation. October, 1898, had catarrh, during which difficulty in coughing, clearing throat and swallowing. Much weaker. January, 1899, right arm too weak to brush hair, recovering after two days' rest. Aching right arm and leg. Easter, 1899, right ptosis became constant. Diplopia. Difficulty in mastication. Worse in great heat or cold, and after exertion or emotion. Almost free from symptoms after rest. Condition on admission: Chest expands less and less with successive breaths. Ptosis both lids. One morning, instead of ptosis, retraction of upper lid till it was commented on, when lid started drooping. When any symptom is remarked upon it becomes exaggerated. When interested in conversation lids move further up than at other times. Pupils oscillate after prolonged convergence. Jaw frequently drops allowing saliva at night to dribble from mouth. Neck muscles by night time cannot support head. Starts writing well, then forms letters badly, finally stops. Right leg easily tired. No muscular atrophy or twitching. Knee-jerk fair. Myasthenic reaction. Death from respiratory failure, January 2nd, 1904.

(5) Male, æt. 40. Admitted to London Hospital under Dr. Wall, February 10th, 1903. "Malaria" fourteen years previously, since which incontinence

of fæces after aperients. January 12th, neck weak, could not hold head straight. Eyelids drooped and arms could not be lifted. Difficulty in deglutition and mastication and in articulation after talking. Occasional diplopia. Nonystagmus. Weak recti, *i.e.*, left externus, right internus. Cannot protrude tongue. Knee-jerk present. February 22nd, attack of dyspnœa, followed by choking when eating. Myasthenic reaction in facial muscles, trapezius, deltoid. April 6th, increasing dyspnœa and inability to cough up mucus. Death from respiratory failure on 7th. For P.M.'s on all five see p. 79.

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Raymond and Sicard.

83.—H., æt. 51, Male. Attacked at beginning 1901. Watched in wards and out-patient department four months. Ptosis, diplopia, paresis of muscles of mastication and deglutition and muscles of neck. Extreme asthenia of upper and lower limbs, though certain movements could be well performed at first. He was soon in the condition of a curarised animal. Electrical reaction of Jolly for three weeks. No muscular atrophy, fibrillary contractions, troubles of sensation, pupils, bladder, or rectum. Slight diminution of tendon reflexes. No history of alcohol or syphilis. Steady improvement to complete recovery in four months, which has continued in spite of exhaustion and deprivation incident to a Congo exploring expedition. While in hospital took thymus and adrenalin, but for four years has adopted no therapeutic measures at all.

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Taylor, J.

85.—Girl, æt. 25. Under Dr. Beevor. Quite well till May last, when difficulty in speaking appeared, becoming more indistinct after talking a little. Reading aloud in a few minutes produces voicelessness. Then difficulty in using hands for fine movements, *e.g.*, picking up pin. Later arms became weak and had difficulty in doing hair. Hands became too weak to pass a needle through cloth. Lower limbs now increasingly weak. She staggered and could not walk far. Occasional diplopia and heavy feeling in eyelids, though no actual ptosis. Reflexes normal. No wasting or visceral disease.

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Leclerc and Savonat.

86.—Domestic servant, æt. 23. Admitted Hôtel Dieu, May 8rd, 1904. Has always been nervous, frequently feeling a "lump in the throat." Found work too hard, began to drop things, had falls with no cause, and became more and more feeble. Occasional facial asymmetry noted. Condition on May 4th, 1904:—"Neuropathic" disposition, weeping readily. Head droops and cannot be held up long. Slight drooping of left eyelid and paresis of left cheek, and labial commissure. Tongue mobile, symmetrical, cannot be put out more than six times. Swallowing, speech, mastication, limbs and hands easily fatigued. Pulse 80. Chronic constipation. Corneal reflex feeble. 6th May, at 7 p.m., choking fit, dyspnœa, cold extremities, irregular pulse, some seromucus expectoration. No abnormal physical signs in lungs. Death at midnight. See list of post-mortems, p. 80.

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Clarke, J. M.

87.—(1) Miss W., æt. 32. Seen first on October 8th, 1903. No occupation. Grandfather died at 60 from "softening on brain," maternal uncle



in an a-ylum at 50. She had influenza in 1898 and 1899. Present illness began with herpes zoster round right loin in November, 1902. Voice nasal, exhausted after ten minutes. Tongue felt weak, while there was no control over lips. Occasional diplopia due to paresis of left externus rectus. Difficulty in swallowing and mastication, especially when tired or if she goes too long without a meal. Cannot talk during a meal, as food goes wrong way. Difficulty in clearing throat or blowing out candle. Cannot whistle. Occasional weakness of hands, especially right, also of neck muscles. Great variation of symptoms, always worse at end of day, when she cannot smile. Face thin, "myopathic," with drooping eyelids and "nasal smile." Slight oscillatory lateral nystagmus. Emotional. Pupils normal. After opening and shutting eyelids several times, the movement cannot be fully carried out. Tongue wasted and tremulous. Patient cannot put it out fully or touch roof of mouth with tip. No atrophy or disturbance of reflexes or sensation. Spoke as if she had "potato in her mouth." Myasthenic reaction in lip muscles, not in limbs. Face muscles to galvanism ACC=KCC. Slight insensitiveness of pharynx. When cold she lost all power in hands. After a month's rest, put on liq. thyroideus, which was followed by immediate general improvement. Ptosis improved and diplopia went. In about seven weeks worse. Dysphagia. Saliva could not be swallowed. Fed by nutrient enemata. Diarrhoea set in after eighteen days. Death from exhaustion. Conscious to end, in three and a half months from when first seen.

(2) Mrs. B., æt. 63. Healthy for age. Illness began one month before. Had been feeling "run down," noticed voice indistinct and difficulty in swallowing liquids or solids. Stomach tube passed easily. Speech more and more indistinct with every effort, which "hurt her in the chest," and at times took away breath. Slight cough; could not expectorate. Muscles of mastication soon tired. After three weeks right ptosis with lacrymation. Past five days failure of sight, pains in right shoulder, and, on one night, diplopia. After repeatedly closing eyelids, right refused to act. Pupils and optic discs normal. No wasting. Soft palate easily tired. Slight insensitiveness of pharynx. Limbs normal. Sudden fatal dyspnœa ten days after. No post-mortem examination.

#### Algyogyi.

83.—Woman, æt. 26. One and a half years ago following a cold she noticed that she tired very easily and could not carry out even easy continuous movements. General weakness of muscles supplied by trigeminal, facial, and hypoglossal nerves and muscles of extremities. Mask-like immobile face. Lagophthalmos. Lateral movements of tongue impossible, difficulty with speech. Electrical reactions normal.

#### Wassing, K.

89.—Girl, æt. 15, Tyrolese. Lost father from phthisis, one sister from tuberculous meningitis. Illness began September, 1900, when haymaking, with fit of dizziness. Recovered after a few minutes and then noticed diplopia. Marked ptosis right and left and convergent squint. Occasional nocturnal enuresis (unknown before). Spoke as if she had something in her mouth. Able to walk a long way over a mountain pass. November 5th, 1900, came to Innsbrück Klinik. Could not whistle. Onset of dysphagia. After seven

weeks in hospital so weak that the slightest walking gave great difficulty. Went home, and ptosis, which had gone, reappeared, with weakness of arms and legs in certain movements. Could not put hands to back of head or lift legs, though other movements free. New Year's Eve, 1901, violent dyspnoea for ten minutes, recurring later on. Breathing slow and feeling of compression of chest. Since 1902 much loss of flesh. Condition steadily worse. Illness now has lasted four and a half years. Latterly scoliosis has developed rapidly. Treatment: faradism, and potassium iodide, internally.

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Raymond and Lejonne.

92.—(1) Mlle. C., æt. 38. Healthy family. Thin. In winter, 1902, sense of cold at nape of neck, and some frontal headache, disappearing in summer to reappear in autumn and become worse in winter 1902-3. October, 1904, temporary feeling of suffocation and loss of speech. Tired easily. December, 1904, for three hours numbness of hands. Could not do hard work, and moved arms with difficulty. Later, weakness of legs, especially after short walking. More difficulty with speech, nasal voice. Symptoms continued much worse in cold or damp, when mastication and deglutition were very difficult, nearly absent in warm dry weather. Admitted into the Salpêtrière, 8th March, 1906. Lagophthalmos. Weak movements of cheek, lip, jaw, and muscle of mastication. Some paralysis of palate, pharyngeal muscles, and larynx. Some permanent paralysis of vocal cords, especially left. Voice nasal. Consonants slurred, especially b, d, s. Extensors of neck kept more power than flexors, causing tendency for head to fall backward if patient attempts to hang forward. Right upper limb weaker than left. Deltoid, latissimus dorsi, and pectoralis especially affected. In forearm chiefly extensors, and in lower limb flexors of hip and knee. Muscles of abdomen and vertebral column weak. Reflexes and sensation normal. Partial myasthenic reaction. Muscles fatigued by repeated stimuli, both galvanic and faradic. Pulse 80. Arterial tension 14-15.

(2) Soldier, "Sergent-fourrier," æt. 26. Recurrent gonorrhœa. During twelfth attack, February 4th, 1906, when "run down" with much late work, noticed ptosis. On February 10th, rapid tiring of hand in writing, and on 11th could not get into a railway carriage, and found all prolonged movement impossible. General weakness. Diplopia on looking to right. Vision indistinct. Difficulty in opening mouth in mastication. Weak, spluttering voice. Increase in symptoms till February 25th, when spontaneous improvement and departure of ptosis. March 22nd, pulse 52; tension 14-15 (Potain's sphygmomanometer). Ptosis. General weakness of eye muscles, especially of externus recti, rapid action of which produces nystagmus. Some paresis of muscles of right side of face. Forward projection of lower jaw weak. Limbs, right more affected than the left, especially muscles of the root, *e.g.*, shoulder, deltoid, psoas. Extensors more than flexors. Rapid fatigue of all muscles. Cervical muscles, anterior and lateral, weak, allowing head to roll forward, also extensors and flexors of vertical column. He cannot sit up without support of hands. Tendon reflexes brisk. No myasthenic reaction, sensory, trophic, or mental disturbance. Sphincters normal.

Guido Bini.

93.—Man, æt. 60, with nervous and alcoholic family history. Following a chill began to notice ready exhaustion of limb muscles, then of those innervated by bulbar nuclei, then rapid exhaustion of vision. Daily variations in fatigue. No myasthenic reaction; no atrophy. Some "contractures" of face muscles giving a "bulbar" expression.

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Charpentier, M. A. "Myasthénie Bulbo-spinale chez un tabétique."

94.—Man, æt. 36. Contracted syphilis at 26. Came July, 1905, for sudden muscular weakness in limbs. Argyll Robertson pupil, and myosis. No right knee-jerk, and both Achillis jerks lost. Some trouble with urine. General weakness, slight paresis of arms, bilateral ptosis, facial paralysis, deviation of tongue, difficulty with speech (unlike that of general paralysis), slight dysphagia. Voice became nasal, articulation defective. Suffocative attacks, paralysis of trunk, lower and upper limbs with muscular atrophy. No myasthenic reaction or reaction of degeneration. Improved under four weeks under injections of calcium and strychnine, and exhibition of Pot. Iod. Movements of arms the first to reappear. To-day, November 8th, 1906, the myasthenia has gone, leaving the tabes. Can the former be dependent on the syphilis, or is it a mere coincidence?

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Muskens, L. J.

98.—De V., woman, æt. 25. Married three months. Trembling arms and legs, progressive. Diplopia. Feeling of oppression in head, and loud noises on right side, rendering hearing bad. Last four weeks unable to walk. All fluids cause choking. No nervous family history. A year ago noticed quick tiring in household work. Eight weeks ago feverish attack. Pains all over body, especially in left knee. Has lately felt as if heavy weight were laid on her chest. Variation in symptoms. Heaviness and impaired mobility of facial muscles and extremities. Face expressionless in laughing and speaking. Voice strongly nasal, with poor movement of palate. Pupils react slowly to light. Lateral movements of eyes limited, and associated with nystagmoid movements. Slight left ptosis. Bilateral exophthalmos. Protrusion of tongue weak. Hands can sometimes be held up thirty seconds; sometimes, especially in middle of day, not three seconds. Reflexes upper and lower limbs exaggerated. Ankle clonus right. Plantar reflex occasionally not obtainable, left occasionally extensor, right doubtful. Swallowing difficult. Pulse 100. February 24th, 1902. Ptosis has been bilateral, and is now slightly less. February 20th, 1904, seen again. Dizziness and feeling as if head were constricted in tight band. Has fallen once or twice. Otherwise great improvement.

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Riggs, C. E.

103.—(1) Male, æt. 37. German. Three weeks before illness occipital pain, worse at night. March 31st, 1902, diplopia, followed in five days by weakness of entire motor system. Could not whistle, swallow or raise left arm, paresis of lower part of face, tongue and frontales. Double ptosis (left and right), ophthalmoplegia externa. Mask-like face with "nasal smile of Gowers." Could only raise upper lip and not move out angle of mouth. Masseters, temporals, and neck muscles weak. Head

occasionally drooped forwards. He could not swallow solids. After talking short time jaw dropped and speech became nasal. Paresis soft palate. Pulse 52-64. Legs soon exhausted. Sensation and reflexes normal. Myasthenic reaction in thighs and legs. Weaker towards evening. October 16th, 1902, ophthalmoplegia went and great general improvement appeared.

(2) Swede, æt. 35. Labourer. In 1899 temporary weakness of lower limbs, possibly due to his alcoholic habits. Perfectly well till February, 1902, when, after severe chill, lips seemed weak at evening. Trouble transient, but reappeared in June, 1902, with dysphagia only in evening and temporary diplopia. Pain in top and back of head. Vertigo. December 31st, 1902, double ptosis. Nasal smile and face expressionless. Ocular fundus normal. Tongue flabby, perhaps slightly wasted, could only be protruded two or three times. Speech very nasal. Soft palate paralysed (right and left). Nasal regurgitation. Salivation. Swallowing better in morning. Emaciation. Knee-jerk sluggish. Soon exhausted, left side. Can walk half a mile. Hands weak after slight exertion. Myasthenic reaction both biceps muscles.

(3) Professor Y., æt. 45. March, 1903, epidemic of scarlet fever in his school. He himself had high temperature for a few days, with no rash. Irritation of eyes noticed after fumigation of rooms with formaldehyde. In April, diplopia; in May, left ptosis. June, weakness of left arm, third and fourth fingers of left hand. July, right ptosis (left began to improve). Right arm weak. August, could not masticate. Both legs weak. Mask-like face. Nasal smile. Could not whistle. Tongue only protruded a few times. Ophthalmoplegia externa. Speech thick after a few minutes. Walked a mile. Dynamometer markings from hand showed rapid tiring. No atrophy or disturbance of sensation. Accumulation of mucus in throat and salivation. Pulse 74-90. Myasthenic reaction left arm. November 18th, attack of tachycardia and dyspnoea, also December 14th. Always better in morning. Death in April, 1904, "from involvement of vagus."

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Johnston, G.

104.—Shown before Neurological Society. Female, æt. 28. Last twelve months difficulty in articulation, gradually worse, especially at night and after sustained speech, when she merely mumbles. Double ptosis (right and left). Marked difficulty in looking up. Lately diplopia. Arms very weak and soon exhausted, whereas lower limbs are not much affected. Walks well, though easily tired.

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Hirschl.

105.—Caroline B., æt. 28. Domestic. One maternal uncle in an asylum, another died hæmiplegic. October, 1903, slight attack of influenza, immediately followed by nasal regurgitation of fluids, and then difficulty in swallowing solids. Shortly after lagophthalmos, left palpebral aperture smaller than right. Patient tired after long speaking. Speech nasal, tongue moved with difficulty. Difficulty in chewing. In March, 1904, extremities involved. Not able to raise hands to do hair, but could wash fairly well. Tired after an hour's walking. Variation in course. No thymic dulness. Slight bilateral ptosis, especially after repeatedly closing lids. After several lateral movements, horizontal nystagmus. Frontalis exhausted by ten attempts to

wrinkle forehead. Paresis both sides of mouth, especially right. Cannot puff out cheeks or whistle. Angular contracture in proximal interphalangeal joints, noticed since age of 12, also in mother and one sister. Knee and Achilles jerks lively, tiring, yet never disappearing. No disturbance of sensation. Myasthenic reaction in frontalis, chin muscles, left third interosseous space and thenar eminence.

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Trömner.

106.—Woman, æt. 50, married to an alcoholic. No history of syphilis. February, 1905, after a winter of emotion and overwork complained of dizziness, palpitation and occipital headache, and three weeks later vertical diplopia. At end of June, bilateral ptosis. Better in autumn. Four weeks before Christmas a series of bulbar symptoms, weakness of chewing, speech and swallowing. After speaking any time tongue became immovable. Nasal regurgitation of fluids. In evening could often chew, nothing solid. December, 1905, marked paresis of all externus ocular muscles, lagophthalmos, paresis of all externus ocular muscles and frontalis. Face sleepy and expressionless. All movements of body weak. No disturbance in reflexes or sensation. No atrophy or reaction of degeneration. After looking up several seconds lids drooped; outstretched tongue was soon drawn back, and arms could only be kept horizontal for three seconds. Myasthenic reaction, especially in supinator longus and trapezius.

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Löser.

108.—Two cases of myasthenia with exophthalmic goitre. See under section "Predisposing causes."

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Boldt.

110.—A. G., æt. 30, country labourer. Admitted to hospital August 7th, 1903. Ob, January 16th, 1904. Ill four months before admission. Gradual onset with diffuse head pains, with weakness and insecurity of legs, causing occasional falls. Arms weak. Speech difficult after talking some time, occasionally unable to close mouth, letting saliva dribble. Difficulty of chewing and swallowing. Strong after a rest and in morning, symptoms set in later. Nutrition good. Signs of earlier hydrocephalus. Knee-jerk exaggerated both sides; ankle and patella clonus. No Babinski's or Romberg's sign. Right pupil a little wider than left, both reacting sluggishly. Fundus and colour vision normal. Drooping of lower lids and epiphora. Crossed diplopia. Facial muscles sluggish. Tongue protrusion slight, and some coarse tremor. Soft palate raised only slightly. Special senses intact. Difficulty in articulation worse for exercise. Blood and electrical reactions normal. After temporary great improvement became worse. October 20th, 1903, severe attacks of dyspnœa. Lagophthalmos worse. November 20th, 1903, remissions shorter. The slightest effort brings on general quivering of whole musculature. December 30th, 1903, no trace of reaction of degeneration, but distinct myasthenic reaction. Breathing laborious, apart from trouble due to falling back of tongue. Variations in strength of pulse. January 8th, 1904, increased dyspnœa. Attacks of suffocation. Edema of left hand and forearm. 16th, death. For post-mortem see list p. 80.

Delile and Vincent.

112.—Girl, *æt.* 21. Health good, except for constipation and dysmenorrhœa. From March to May increasing sense of general fatigue. July, after very abundant period, nasal voice, weakness both hands. Better in August. In September, painful menstruation and great increase in sense of fatigue. Bilateral ptosis, weakness of neck and lower limbs. Paresis of soft palate. Difficulty in rising from decubitus. Troubles worse after movement. Electrical reactions normal, also reflexes and sensation. In October great weakness. Dysphagia. In November, following results of M. Renou and Delile on opotherapy (*Soc. de Thérapée*, 22nd January, 1907), we gave powdered hypophysis and ovary. Pulse previously 96–110, tension 15. Blood normal (reds 3,600,000, leucocytes 64,000, H.B. slightly diminished), afterward pulse 64–74, tension 16–22. General steady improvement. Left hospital 22nd December, and by 5th February quite strong. Blood count, reds 4,800,000, whites 9,600. Normal hæmoglobin.

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Tilney, F.

113.—Harriet W., *æt.* 24, married. Primipara. Pregnant nine months. Dizzy since commencement of pregnancy, and weak in arms. Dysphagia. Loss of voice, stiffness of jaw muscles. Attacks at varying intervals, being fairly well in between. September, 1905, diplopia. Chokes easily. Cardiac apex in sixth space, nipple line. Pulse 70. After successful confinement attacks continued. Fatal attack of dyspnœa February, 1906, after nine months' illness. For post-mortem findings see p. 80.

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Barnes, S.

115.—Woman, *æt.* 38. Onset with difficulty in swallowing and great fatigue after speech. Rapid tiring after movements of limbs and in evening ptosis and diplopia. Great weakness of muscles of left side of face. Atrophy of masseters and temporal muscles.

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Macintosh, A. W.

116.—Woman, *æt.* 31. Started with bulbar symptoms, followed by extension of symptoms to muscles of limbs. Double ptosis and ophthalmoplegia externa, paralysis of upper facial muscles and muscles raising lower jaw. Difficulty in articulation, mastication, and respiration. Death from pneumonia after several attacks of syncope and difficulty in respiration.

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Fabrio, Pietro.

117.—Woman, *æt.* 30, worn out by frequent pregnancies, work, and wretchedness. First symptoms in ocular muscles, *i.e.*, left ptosis and paresis of left external rectus, followed by weakness of other motor muscles of eyes. Then difficulty in mastication, with pain in masseters and temporals, and tinnitus. Nasal voice and crises of dyspnœa. Weakness and atrophy of muscles of neck, shoulders and arms came on later. No reaction of Jolly or of degeneration.

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Frugoni, C.

118.—Typical case with all the symptoms. After two years' illness died of pneumonia. For P.M. see list. Nothing pathological in central nervous system except an accidental anomaly in floor of fourth ventricle. Cell foci in muscles.

## Von Rad.

120.—Girl, æt. 22, in June, 1906, left ophthalmoplegia externa, and slight paresis of right abducens. Headaches, dizziness and slight incontinence of urine. Reaction to light of right pupil slow. After temporary disappearance of ocular symptoms, diplopia in February, and dysphagia, increasing during meal. Speech indistinct. Incontinence disappeared. Arms and legs tired readily. Double facial paralysis, features being mask-like and very slow in movement. Movements of jaw slow and weak. Only fluids could be swallowed, and that with difficulty. Salivation. Nasal regurgitation. After counting forty, speech very indistinct. Movements of tongue good at first, soon tired. Sensation and reflexes normal. No atrophy. Marked myasthenic reaction in both sterno-mastoids, and to lesser degree in deltoids.

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Grund, C. "Ein auf Rumpf und Extremitäten beschränkter Fall von M. G."

121.—H. F., boy, æt. 10. In 1900, at age of five, had diphtheria, and spent fourteen days in bed, getting well after four weeks. Four weeks later, frequent falls and weakness of knees noticed. Walk became worse till, in one year, he could hardly walk. Six months later improvement, though he could not make long excursions. In 1904 much worse, fell down after a few steps, and became weak in arms and hands. Writing unaltered and strong. In 1905 occasional squint and temporary diplopia. Lordosis in lumbar region. Trapezius and rhomboids very weak, also serratus anticus, infra-spinatus, deltoid, flexors of elbow, supinator longus, triceps, muscles of abdomen and hip, glutei, quadriceps, flexors of knee. Slight wasting of shoulder muscles. No reaction of degeneration. Myasthenic reaction at first absent, later appeared well in extensors of forearm and quadriceps. Face and jaw free. Slight horizontal nystagmus on extreme lateral movement of eye. Later, occasional temporary divergent strabismus, with diplopia. Symptoms better in bed, coming on soon after getting up.

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Paul, W. E.

122.—A. L., æt. 26, widower. Eight years ago had hard chancre, and treated for twenty-four months. Occasional excess in tobacco and alcohol. Eighteen months ago, in the course of a severe cold, myasthenic symptoms developed in arms, followed within a month by symptoms in face, eye, chewing, swallowing, and in many muscles of trunk, and in all extremities. Sphincters and sensation free. Reflexes active, and knee-jerk could not be exhausted. No myasthenic reaction. Death at end of May, 1907.

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Chvostek.

123.—Lady, æt. 32. Treated for years for nervous symptoms. In 1904, after nursing her mother in her fatal illness, changed much for the worse. Obstinate constipation and severe anæmia. Went to Brazil, where, apparently, she suffered from dysentery. This was followed by increase of nervous symptoms, sleeplessness, depression, violent headaches, and pains in limbs, swelling of face and legs, falling out of hair. Several months later, rapid fatigue in walking; evening diplopia. Speech unintelligible after talking, occasional dysphagia. On her return to Europe she showed swollen

lips, swellings under chin, not pitting on pressure, thickness of skin of lower extremities, mental apathy. When patient looks up eyelids sink more and more till they cannot be raised. Speech at first good, soon becomes impossible. Easy fatigue of walking and finger movements. Knee-jerk gradually weaker. Myasthenic reaction in flexors of fingers and quadriceps cruris. Gradual disappearance of symptoms under thyroid treatment till no symptoms of myasthenia or myxœdema remain. When last seen, October, 1907, quite well.

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Guthrie, Leonard.

124.—(1) Woman, æt. 23, single. General weakness, especially in speech and deglutition. Aunt suffers from epilepsy, sister from "chorea gravidarum." Healthy till December, 1898, when tired feeling began. Poorness of speech from inability to use lower jaw properly. Deglutition bad. Liquids ran back through nose. She could not close eyes, and found fingers of right hand dropped. Symptoms worse on emotion. January, 1900, could not walk alone. Speech unintelligible. Paresis of orbiculares oris and palpebrarum, tongue and soft palate. No nystagmus or squint. Speech weak and nasal, unintelligible after a few minutes. Cords normal. Food collected in cheek. Loss of muscle power only after exertion and disappearing after rest. Reflexes, sphincters, sensation and muscle sense good. Electrical—slight reduction to faradic stimuli. Myasthenic reaction. Right biceps ceased to react to faradism in one minute, response returning in 15–20 seconds. Reaction less in lower limb. With rest and strychnine improved, and left hospital. June, 1900, relapse, much dysphagia, weakness of neck muscles. July 11th, dyspnoic attack. Fed per rectum. 15th, apparent diaphragmatic paralysis. Death. See list of post-mortems p. 80.

✓ (2) Boy, æt. 11 years. In-patient at Regent's Park Hospital, April, 1893, under Dr. Bennett. Diagnosed by Dr. Guthrie as diphtheritic paralysis with no history of diphtheria, and by Dr. Bennett as dysphagia and nervous debility. Discharged much improved. Re-admitted April, 1894, with general feeble action of face muscles, paresis of both orbiculares and frontales. Pupils dilated. Cannot whistle or pout lips; tongue weak, voice nasal. Weakness of upper and lower limbs, especially trapezius and deltoids. Knee-jerk sluggish. Facial muscles react fully to faradism. Attacks of dyspnoea commenced on April 25th, continued, and caused death May 24th. See list of post-mortems.





# A CASE OF TRAUMATIC RUPTURE OF THE NORMAL SPLEEN; SPLENECTOMY.

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By

C. H. FAGGE, M.S.

AND

H. C. MANN, M.D.

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ANNIE, F. aged 13, was admitted on July 9th, 1906, in an unconscious condition, having been knocked down by a motor-car. There were bruises on her face and head, and on recovering consciousness she complained of pain over the shoulders, arms, and body. When examined on the following morning the abdomen was found to be rigid, tender and distended, these signs being most marked in the upper part and left side of the abdomen. There was no evidence of free fluid in the peritoneal cavity. The patient was restless and extremely pale, the pallor, which at first had been put down to the shock resulting from the accident, having increased rather than diminished during the night. The temperature was 97°, pulse, faint (132), respiration 32.

*Operation.*—Under a general anæsthetic a longitudinal incision was made in the abdomen, in the middle line, about six inches long. On incising the peritoneum the bowels protruded, and a large quantity of dark blood escaped. At this stage it was thought that one of the solid viscera in the upper part of the abdomen had been injured, so the hand was passed into the abdomen and the liver explored. It was then found that clots

and fluid blood were welling up to the wound from the left side of the peritoneal cavity, and further digital exploration made it clear that the spleen was the seat of the hæmorrhage. There was much extravasation of blood into the gastro-splenic omentum, and the spleen was felt to be almost divided in two. This was carefully drawn into the wound, the pedicle being meanwhile controlled by the fingers, and artery forceps applied to it. As the spleen was almost bisected by a transverse wound, it was considered impossible to deal with it by any other method than by excision. The pedicle was therefore quickly ligatured with stout catgut, and the organ removed. When the torn spleen was first brought up into the abdominal wound, it was seen that there was a spleniculus about three-quarters of an inch in diameter lying attached to the gastro-splenic omentum, about two inches above and internal to the spleen. In ligaturing and removing the spleen itself, care was taken that this was in no way interfered with. The left hypochondrium was now rapidly cleared of clots with sterilised pads wrung out in normal saline solution, but no special attention was paid to this detail, as it was felt that rapid closure of the abdomen was more important to the patient, now that the cause of the hæmorrhage had been dealt with, than careful removal of all blood, which must have entailed the expenditure of several minutes. The protruding intestines were returned to the abdominal cavity, into which as much saline solution as possible was quickly poured, and the abdominal wound was closed with one layer of stout salmon-gut sutures. During the latter part of the operation saline infusion was begun, as at this time the radial pulse could scarcely be felt. One pint was introduced subcutaneously during the operation, and three pints were given during the afternoon. Strychnine and adrenalin hypodermically were freely used during the forty-eight hours after the operation.

In the evening the temperature was 98°, the pulse 140, the respiration 44. On the following day the patient was conscious, and the radial pulse could be distinguished. She vomited during the following morning, but complained of no pain. In the evening the temperature rose slightly above normal; the pulse



*A Case of Traumatic Rupture of the Normal Spleen ; Splenectomy.*



was 112-132, the respiration 20-28. After this date the general condition improved, the sickness gradually disappeared, and the patient was discharged from the hospital on August 20th, 1906.

The recovery from a condition of extreme collapse, owing to the loss of a large amount of blood, was uneventful. Repeated examination failed to discover any enlargement of the lymphatic glands in the axillæ, neck, or groin.

#### REMARKS BY MR. FAGGE.

The point in this case which appears to me to be most interesting is the presence of the spleniculus, and the question naturally arises as to whether the recovery of the patient without any of those untoward consequences which have been recorded by Pitts and Ballance (*Clin. Soc. Trans.*, vol. xxix., p. 77) after excision of the spleen was in any way due to the presence of this spleniculus, which it might be supposed would gradually hypertrophy and undertake the functions of the removed organ. And in this connection it is interesting to note that the above symptoms, namely, progressive anæmia, abdominal pain, thirst, drowsiness, feebleness, and marked changes in the blood, one or other of which occurred in two of Pitts' and Ballance's patients, were not met with in the third case, a boy of ten, in whom a spleniculus was found at the operation, though my case differs from Mr. Ballance's patient in that the latter was found to have enlargement of the cervical, axillary, and inguinal lymphatic glands at a period of five months after the injury.

The diagnosis of a ruptured spleen was not, in this case, arrived at before the operation. All that could be said with certainty was that the patient was suffering from collapse, due probably to internal hæmorrhage, as some ten hours had elapsed since the accident, so that the period in which such symptoms might have been put down to shock had long since passed by. Again, there was no evidence of any extensive fracture, either of the ribs or pelvis, which might have been responsible for the patient's condition.

In the notes of the case it was pointed out that there was no evidence of free fluid in the abdomen, and no increased dulness

was detected in either hypochondrium. Pitts and Ballance (*loc. cit. supra*) emphasise the importance of an increase of dulness in the splenic region, which does not alter with the position of the patient, while any increase of dulness in the right flank can be made to disappear on turning the patient on to his left side. These physical signs, in their opinion, are very suggestive of hæmorrhage due to injury of the spleen, and I regret that in the above case attention was not paid to this physical sign, but I was not at the time aware of its significance.

It is very difficult to be dogmatic as to the right line of treatment to be adopted for cases of ruptured spleen in general. The question can only be answered for each individual case at the time of operation, and it is generally agreed that excision alone will provide the two desiderata—namely, to stop the bleeding and prevent its recurrence—when, as in the above case, the organ is almost completely torn across. In these cases, as in other operations for extensive intra-peritoneal hæmorrhage such as follows ruptured extra-uterine foetations, no importance need be attached to the careful removal of all clots from the peritoneal cavity.

Pitts and Ballance advise that, in dealing with intra-abdominal hæmorrhage of doubtful origin, a central exploratory incision should be made first, and when the source of the bleeding has been localised a second lateral incision should be made in a more favourable position. When, as in the above case, the mesenteric attachments of the spleen are sufficiently long to allow this organ to be drawn up into a median abdominal wound, a second incision seems scarcely necessary, and, provided that operating through the central wound does not make ligature of the splenic pedicle more tedious, and leaves no doubt in the operator's mind that all bleeding points have been secured, a second incision will only have the disadvantage of requiring time, even though only a few moments, for its suturing.

Fortunately, in my case, the most difficult question which the surgeon is called upon to decide in the treatment of these cases had decided itself before I saw the patient. This is the choice as to the most suitable period after the injury for the performance of such an operation as abdominal section. Looking over this

case afterwards, I am inclined to doubt whether even a provisional diagnosis could have been arrived at at the time the patient was admitted to the hospital. In fact, it was not until some hours had elapsed, and the collapsed condition of the patient increased rather than diminished, that intra-abdominal hæmorrhage was suspected.

*Prognosis.*—Mr. Graham Simpson, in recording a successful case of splenectomy for ruptured spleen (*Clin. Soc. Trans.*, vol. xxxix., p. 33), has collected 70 cases of ruptured spleen between 1891 and 1905. Of these, 42 were operated upon, and 27 lived. Berger (*Bergmann's Surgery*, vol. iv., p. 702) collected records of 130 operations for this condition, which were followed by recovery in 77 cases.

#### REMARKS BY DR. H. C. MANN.

The following blood counts were made upon the case :—  
1906.

July 10th. Leucocytes, 12,000 per cubic mm.

July 16th. Leucocytes, 10,500 per cubic mm.

Hæmoglobin, 60 per cent. (Haldane's hæmoglobinometer).

Differential count. There were counted 144 leucocytes. Of these there were :—

78 Polymorphonuclear.

45 Small lymphocytes.

10 Large lymphocytes.

8 Indeterminate.

3 Eosinophiles.

Giving the following percentage :—

Polymorphonuclear, 54 per cent.

Small lymphocytes, 31 "

Large lymphocytes, 7 "

Eosinophiles, 2 "

July 20th. The following count was made :—

Red cells, 3,280,000 per cubic mm.

Leucocytes, 8,400 per cubic mm.

Hæmoglobin, 65 per cent.



July 23rd.	Leucocytes, 8,400 per cubic mm.
	Red cells, 3,330,000 per cubic mm.
	Hæmoglobin, 66 per cent.
July 30th.	Leucocytes, 8,320 per cubic mm.
	Red cells, 3,560,000 per cubic mm.
	Hæmoglobin, 70 per cent.
Aug. 4th.	Leucocytes, 6,850 per cubic mm.
	Red cells, 5,200,000 per cubic mm.
	Hæmoglobin, 81 per cent.
Dec. 3rd.	Leucocytes, 7,200 per cubic mm.
	Red cells, 5,125,000 per cubic mm.
	Hæmoglobin, 95 per cent.
	Differential count :—
	Polymorphonuclear, 65 per cent.
	Small lymphocytes, 26     "
	Large lymphocytes, 5     "
	Eosinophiles, 4     "

In most of the cases of splenectomy for ruptured spleen which have been described, very similar changes in the composition of the blood, as detailed above, have been found.

There is an initial leucocytosis, a fall in the percentage of hæmoglobin, and a diminution in the number of red cells, a recovery to normal occurring within about six weeks of the operation. The early leucocyte count has usually shown about 12,000 leucocytes per cubic millimetre, sometimes within a few hours of the operation, though this may follow the induction of anæsthesia quite apart from the nature of the operation performed. The fact that there was a speedy return to normal, in the above case, is explained partly by the fact that the patient was a child, and still more so by the presence of a spleniculus, which was observed at the time of operation. For some time after the operation, a differential count shows that the lymphocytes are actually and relatively increased in number, and the above case was no exception to this rule. No enlargements of lymphatic glands were noticed when the child was examined about five months after the operation, though such changes have been

found in other successful cases. Any theories as to the possibility of such enlarged lymphatic glands carrying on splenic functions do not appear to us to rest upon a sound basis. The presence of accessory splenic tissue in the abdomen is certainly far commoner than is generally supposed. The demonstrator of morbid anatomy who dissects carefully along the course of the splenic vein will frequently find masses of splenic tissue varying in size from a pea to a walnut. The presence or absence of such spleniculi may possibly explain the variations which have been noticed in the blood-count, and in the general progress of the case after splenectomy has been performed.

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Since writing the above, I have to-day (August 19th, 1908) examined the patient, who is now a healthy-looking, chubby girl, though perhaps rather fatter than is usually considered to be within normal limits. Mentally she is bright and active. Her blood, both numerically and qualitatively, shows a normal count:—Polymorphonuclear leucocytes, 68 per cent.; hæmoglobin, measured both by Talquist's and Haldane's methods, works out at practically 100 per cent. No glands were found to be enlarged or unduly palpable; the scar of the incision is firm, and is about the width of a split straw; the parietes are freely moveable on the underlying intestines.



# PERITONEAL ADHESIONS IN A SERIES OF FIFTY CONSECUTIVE POST-MORTEM EXAMINATIONS.

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By

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AND

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IN routine post-mortem examinations the condition of the intestines and of the enveloping folds of peritoneum is seldom examined *in situ*. After removal of the intestines from the abdominal cavity, the peritoneal relations are destroyed, together with any bands or adhesions which may have been present. From the post-mortem records of the hospital it is, therefore, impossible to gain information as to the presence or absence of peritoneal adhesions, or to calculate their frequency.

Since great importance has been ascribed to these adhesions by some writers, who have regarded them at one time as the cause, at another as the effect, of chronic constipation, it has been thought worth while to record the conditions observed in a series of consecutive post-mortem examinations. Fifty cases were examined. No selection was made, but obviously unsuitable cases were excluded, as, for example, cases of suppurative or of tuberculous peritonitis. The ages of the cases, therefore, varied from three weeks to sixty-eight years. In addition, the condition of the peritoneal folds was examined in six fetuses. The usual post-mortem incision was made from under the chin to just

above the symphysis pubis; the costal cartilages and sternum were removed, and the abdominal muscles cut transversely so as to allow of a full examination of the flanks. The bodies, which had been preserved in a freezing chamber, were examined always within twenty-four hours of death, and in many cases within a much shorter time.

*The appearance of the adhesions.*—In their most marked form the adhesions were quite unmistakable, and caught the eye at the first glance. They consisted of dense fibrous bands of a glistening white colour. In slighter degree the adhesions consisted of a line of thickening and opacity in the peritoneum. At times these slighter adhesions were apt to be simulated by folding of the peritoneum along lines of traction, but these folds, unlike the true adhesions, could always be obliterated by release of the tension or by a little manipulation.

It is of course impossible, from a simple examination of the structure of these adhesions, to determine the causes which have produced them. Yet it may be remarked that their appearance was not generally suggestive of the matting which results from former acute inflammation of the peritoneal folds. The bands were almost invariably of some length, so that they formed rather suspensory ligaments than true adhesions, if by the latter word is implied abnormal contact of surfaces. The frequency with which the bands were found stretching in parallel lines, often with a uniform obliquity, as well as the similarity between the smaller and less definite adhesions, which were yet permanent and ineffaceable, and folds of peritoneum along lines of tension which could easily be obliterated, certainly suggested that the adhesions were the result of traction of the gut along definite lines of force.

*Age.*—The youngest case was three weeks old, the oldest sixty-eight years. No fewer than seventeen cases were under five years of age.

The frequency of adhesions varied to a considerable extent with the age of the subject. The number of adhesions was generally greater in adults, and the adhesions were, as a rule, of greater strength and density. Moreover, in the seventeen children of five years of age and under examined, six were quite free from

adhesions. In the remaining eleven children perfectly definite adhesions were found, and they were present in the youngest case. On the other hand, no adhesions were found in any of the seven fetuses which were examined.

*Sex.*—Twenty-eight were males, twenty-two females. Adhesions appeared equally frequent in both sexes. In one case only (21) did they appear to take origin in the female pelvic viscera. Adhesions attached to the gall bladder were more common in adult males—nine cases out of nineteen—than in adult females—three cases out of thirteen. The appearance of these adhesions did not suggest that they were due to former inflammation of the gall bladder. If such had been the cause, the greater frequency of cholecystitis in the female sex should have been obvious.

*The position of the adhesions.*—Except in the last few inches of the ileum, no adhesions were found throughout the small intestine. They were found around the pylorus, around the gall bladder, and with great uniformity in various parts of the large intestine.

*The cæcum, appendix, and ascending colon.*—In this part of the gut adhesions were found most frequently of all. They were present in greater or less degree in thirty-five cases. The bands were commonly in two positions. A group could be recognised passing from the blind extremity of the cæcum downwards and outwards to the iliac fossa. A second group commonly passed from the lower part of the ascending colon and cæcum obliquely upwards and outwards to the postero-lateral aspect of the abdominal wall. These latter were the longest adhesions observed. In most cases they could be traced on to the anterior aspect of the gut. They lacked the density and strength as well as the glistening whiteness of the bands observed in the sigmoid flexure. They were distinctly vascular and indistinguishable from the normal peritoneum in colour. In spite of the almost constant presence of adhesions, the cæcum contained solid palpable fæces in only three cases. As a rule it was distended with gas.

*The appendix* varied enormously in length and position. It was found free from adhesions in all but three cases.

*The hepatic flexure.*—Adhesions were seldom found binding this flexure to the abdominal wall, but in fourteen cases there

were well-marked bands passing across from the ascending colon inwards to the transverse colon, in such a way as to fix the flexure at a very acute angle. In case No. 24, symptoms of intestinal obstruction, supervening upon a laparotomy, were thought to be due to the kinking caused by these adhesions. In ten cases bands passed from the gall bladder or liver to the neighbourhood of the hepatic flexure.

*The transverse colon.*—In all cases the loop of the transverse colon was convex downwards. In most cases the line followed was roughly that of the great curvature of the stomach with a gentle sweep across the abdomen.

In three children the first part of the transverse colon, by reason of the shortness of the normal peritoneal fold, was held in close apposition to the pylorus. Beyond this the gut descended abruptly in a V-shaped loop for a various distance towards the pelvis.

In two cases the apex of the loop of the transverse colon reached to within an inch of the symphysis pubis.

*The splenic flexure.*—In all cases the fold of peritoneum known as the phrenico-colic ligament, which passes below and supports the spleen, was present. It differed, however, greatly in size and form. Sometimes it was adherent to the spleen, sometimes it broadened out to gain an additional attachment to the postero-lateral abdominal wall along a vertical line.

*The descending colon.*—This was usually found lying as a contracted tube closely adherent to the posterior abdominal wall. Where adhesions were found (ten cases) they were in the form of parallel groups of short bands passing transversely outwards, separated by nearly equal intervals, and were usually in series with more dense bands about the sigmoid flexure. In only one case (45), was a definite mesocolon found.

*The sigmoid flexure.*—Adhesions were found in thirty-one cases and attained a greater density and strength than elsewhere. Under normal circumstances the sigmoid flexure, or, to adopt the newer name, the iliac colon, gradually acquires a mesentery as it passes downwards. The pelvic colon normally is possessed of a mesentery of sufficient length to allow the gut when distended to

rise out of the pelvis. This mesentery is attached along a line shaped like an inverted V, which opens downwards to form the intersigmoid fossa. In the most marked cases of adhesion no trace of this arrangement could be found. The iliac colon lay bound to the iliac fossa, and the pelvic colon could not be drawn from the pelvis. In even the slightest cases the free mobility of this part of the gut was interfered with. The bands were commonly short, not more than one inch in length, and of great strength. In cases 24 and 32 a band passed from the convexity of the omega loop to the root of the mesentery and the termination of the ileum.

*The ileum.*—In addition to the adhesion to the pelvic colon just mentioned, nine cases showed adhesions passing from the end of the ileum to the right iliac fossa.

*The pylorus.*—In six cases there were adhesions passing from the pylorus to the gall bladder and under-surface of the liver. In addition its occasional close relationship to the first few inches of the transverse colon has been remarked.

#### CONCLUSIONS.

1. Peritoneal adhesions were found in a series of fifty consecutive cases, varying in age from three weeks to sixty-eight years, in all but five. They were not found in any of six fetuses.

2. Although becoming more common and of greater degree in adult life, adhesions were found at all ages, even in the youngest case examined.

3. In nearly all cases the large intestine only was involved. The cæcum and ascending colon were the commonest sites.

4. Adhesions were found with such frequency and in such young subjects as to make it difficult to believe that they were either the cause or the result of chronic constipation.

5. No evidence of fæcal accumulation or of stasis in the cæcum was found. Even when adhesions were most marked the cæcum contained only gas.

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The following table gives a detailed account of the condition found in each case:—



Case.	Age and Sex.	Cæcum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
1	F 35	Empty	Band up from upper part	Tied to asc. colon	As usual	—	Tied to iliac fossa	—	—	Sudden death: phthisis, pneumothorax	—
2	F 36	Empty: band to pelvic brim	Long band up and out	Tied to asc. colon by one long band	Do. ...	—	Bands to iliac fossa	—	—	Mitral stenosis	—
3	F 54	Empty ...	Bands up and out	V-shaped, lowest part 1½ in. above pubes	As usual	Band fastening trans. to desc. colon across angle	Fixed to iliac fossa	Fixed to pelvic wall	—	Broncho-pneumonia.	—
4	M 47	Contracted: contained faeces: fixed to iliac fossa	Bands up and out from lower part	—	Do. ...	—	Fixed to iliac fossa	—	—	—	Hepatic flex. fixed to gall bladder, and pylorus fixed to gall bladder
5	M 46	Contracted: slight amount of faeces	—	—	—	—	—	—	—	Cirrhosis of liver	The whole meso-colon and mesentery short. No definite bands. Pylorus fixed to neck of gall bladder.

Case	Age and Sex.	Cæcum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
6	F 39	Empty	...	Bands passed up and out from lower part	Band out and down to ileo-cæcal junction	As usual	—	Single band to brim of pelvis	Bound to pelvic wall	—	Pylorus fixed to gall bladder.
7	F 35	Empty; bound to iliac fossa	Broad band passed up and out	—	Do. ...	—	—	—	Bound to iliac fossa	General peritonitis	Hepatic flex. to pylorus by a band. Hour-glass stomach.
8	F 10	Empty; fastened to brim of pelvis	Broad band passed up and out	A band to neck of gall bladder	Do. ...	Marked bands passed outwards	Firmly bound to fossa	Fixed to pelvic wall	—	Mitral regurgitation.	—
9	F 40	Empty	...	—	Do. ...	—	One band to iliac fossa	—	—	Oxalic acid poisoning	Very fat body. Hepatic flex. fixed to gall bladder.
10	F 3	Empty	...	Slight band passed up and out	Do. ...	—	One thin filament to iliac fossa	—	—	Diphtheria	—
11	M 1 mth	Empty	...	—	Do. ...	—	—	—	—	Cellulitis of thigh	—
12	M 6 wks	Empty	...	Lower part fixed to iliac fossa by band	Do. ...	—	Few bands to iliac fossa	—	—	Broncho pneumonia	—

Case	Age and Sex.	Cæcum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
13	F 50	Empty: bands to iliac fossa	Bands passed up and out from lower half	—	As usual	—	Bound down to iliac fossa	Immobile from adhesions	—	Sudden death. Fibroid heart	Appendix bound by adhesions behind cæcum.
14	M 40	Contained gas and slight amount of feces	Thin bands passed up and out	Lay in pelvis. Strands passed to asc. colon	Do. ...	—	Bound down to iliac fossa	—	Fixed for 4 in. to brim of pelvis	—	Hepatic flex. fixed to gall bladder. Liver fixed to diaphragm.
15	F 30	Empty: turned up in front of asc. colon	Thin bands passed to iliac fossa	Fixed to asc. colon: a kink	Do. ...	Few bands	Bound down to iliac fossa	—	—	—	—
16	M 24	Empty ...	—	—	—	—	Several bands to iliac fossa	—	—	—	Hepatic flex. to gall bladder. Appendix very long and narrow behind colon.
17	F 16 ms	Empty ...	Long meso-colon	—	—	Some-what fixed in lower part	—	—	—	General tuberculosis	—
18	M 7 ms	Empty ...	Bands passed up and out	—	—	—	—	—	—	Marasmus	—
19	F 50	Empty ...	—	—	—	—	—	—	Bound to right pelvic brim	Cirrhosis of liver	Very fat body. Whole mesentery shortened and sclerosed, no definite bands.

Case.	Age and Sex.	Caecum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
20	M 50	Empty: fixed to iliac fossa at blind end	Bands from lower part passed up and out	Fixed to asc. colon by bands across angle	As usual	—	Bound down to iliac fossa	—	Bound to pelvic brim	Early general peritonitis from perforated duodenal ulcer	Band from pylorus to gall bladder.
21	F 1 yr	Empty ...	—	—	Do. ...	—	—	Bound to left ovary and tube	—	Diphtheria	—
22	M 68	Empty: with single band to iliac fossa	—	—	Do. ...	—	Firmly bound down to iliac fossa	—	—	Aortic stenosis	Concretion in appendix.
23	M 34	Empty: fixed down to iliac fossa, one band towards femoral ring	Fine filaments passed up and out	—	Broader than usual	—	Bound to iliac fossa	—	—	Fatty heart. Fatty liver.	—
24	M 45?	Empty: fixed by blind end to iliac fossa	—	Fixed firmly to asc. colon, producing a kink	As usual	Few bands outwards	Cut off short for colotomy	—	—	Operation for carcinoma recti. Symptoms of obstruction after operation. Some peritonitis	—
25	M 34	Empty: tied down at end	Bands passed up and outwards	Fixed to asc. colon across angle	Do. ...	Few bands	Bound to fossa	Bound down	Bands to brim of pelvis	—	—

Case	Age and Sex.	Cæcum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
26	F 2	Empty	—	—	As usual	—	—	—	—	General tuberculosis	—
27	F 3 wks	Empty: filament towards femoral ring	Bands passed up and out	Just past flexure, band to gall bladder	Do. ...	—	Slight bands to iliac fossa	From convexity of loop a band to lower end of ileum	—	Marasmus	—
28	M 3 ms	Empty	—	—	Do. ...	—	—	—	—	Marasmus	Thickening of recto-vesical folds.
29	F 2	Empty	Bands passed up and out	Proximal part fixed to pylorus: distally a V-shaped loop	Do. ...	—	—	—	—	Diphtheria	—
30	M 40	Empty	Bands passed up and out	—	Do. ...	—	Bands to iliac fossa	Band to pelvic wall	—	Cirrhosis of liver	Great omentum fixed to anterior abdominal wall below on left side.
31	F 35½	Empty	Bands passed up and out from lower part	Fixed across angle to asc. colon	Do. ...	—	Do.	—	—	Mitral stenosis	—

Age and Sex.	Cæcum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
32 M 68	Empty: band outwards to lat. wall	Bands passed up and out from upper part	Tied to asc. colon across angle	As usual	—	Bound to fossa	Bound to pelvic wall, also a band to small intestine	—	Fibroid heart. Nephritis.	—
33 M 56	Empty: tied to iliac fossa	—	—	Do. ...	No mesocolon	—	Bound to pelvic brim and wall	—	Street accident	—
34 M 1 yr	Empty ...	Bands passed up and out	—	Do. ...	—	Lay across in the right iliac fossa	—	—	General tuberculosis	—
35 F 34	Empty: many bands down to iliac fossa	Broad band passed up and out: also from hepatic flexure	Fixed by strong bands to asc. colon	Do. ...	Bands up and out	Bound down as far as brim of pelvis	—	—	Tuberculous peritonitis	—
36 M 56	Empty: bands down and out to iliac fossa	Bands passed from upper part	Fixed to asc. colon	Do. ...	—	—	—	—	—	Great omentum fixed to right loin region by a strand. Hepatic flexure to liver.
37 M 1½	Empty ...	Thin band passed up and out	Fixed by a definite band to pylorus	Do. ...	—	—	—	—	Marasmus	—

Case	Age and Sex.	Caecum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
38	M 63	Empty ...	Bands passed up and out	Bands across angle	As usual	Few bands	Bound to iliac fossa, especially to inguinal region	—	—	—	Hepatic flex. to liver and pylorus to liver.
39	M 54	Empty: bound to iliac fossa	Bands passed up and out from lower part	Tied to asc. colon	Do. ..	Bands outwards	Firmly bound to iliac fossa	Firmly bound down	—	—	—
40	F 2	Empty ...	Slight bands passed up and out	—	Do. ...	—	—	—	—	Broncho pneumonia	—
41	F 2	Empty: bands up and out	—	Tied to asc. colon	Do. ...	—	—	—	—	Burns	—
42	M 36	Empty and contracted. Firm band to iliac fossa	Firm band passed up and out from lower part	—	Do. ...	—	Bands to iliac fossa	—	—	Secondary hemorrhage from femoral artery	—
43	M 3 ms	Empty ...	—	Held up to pylorus	Do. ...	—	—	—	—	—	—
44	F 51	Empty ...	Fallen down: only held to gall-bladder	—	Do. ...	—	Bands to iliac fossa	Bands to pelvic wall	—	Died from recurrence after kidney growth removed.	Appendix embedded in adhesions.
45	M 2 ms	Small and contracted	—	—	Do. ...	Long meso-colon	—	—	—	—	—

Case	Age and Sex.	Cæcum.	Ascending Colon.	Transverse Colon.	Splenic Flexure.	Descending Colon.	Sigmoid.	Pelvic Colon.	Ileum.	Cause of Death.	Remarks.
46	M 56	Contracted ...	Extensive bands passed up and out: also to gall-bladder	—	As usual	Few bands	Bound down	Bound down	—	Cerebral tumour.	—
47	M 5	Empty: few thin bands up and out	—	—	Do. ...	—	—	—	—	Sudden death	Large mesenteric glands. Large thymus.
48	M 2½	Empty ...	—	—	Do. ...	—	—	—	—	General tuberculosis	—
49	M 50	Empty bands to iliac fossa	—	Bands to asc. colon	Do. ...	Few bands	Bands to iliac fossa	—	—	Pulmonary hæmorrhage	Great omentum to anterior abdominal wall.
50	F 34	Empty: few bands	Few bands passed up and out	—	Do. ...	—	Few bands to iliac fossa	—	—	—	Scar appearance in peritoneum about duodeno-jejunal flexure.





# SOME OBSERVATIONS ON SPLENOMEGALIC POLYCYTHÆMIA.\*

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By

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AND

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SINCE the introduction of modern methods for the differential staining of the various morphological elements of the blood, the only material advance which has been made in our knowledge of hæmatology has been by the use of the method of determining the total amount of hæmoglobin (total oxygen capacity) and the volume of the blood described by Haldane and Lorrain Smith<sup>1</sup> in 1900. As is well known, the method consists in the administration of a known quantity of carbon monoxide to the subject of experiment and the subsequent colorimetric determination of the proportion of the hæmoglobin which is combined with carbon monoxide. By this means the total capacity of the blood and immediately adjacent hæmoglobin for carbon monoxide may be determined; this is the same as its capacity for oxygen. If, for

<sup>1</sup> Journal of Physiology, vol. xxv., 1900, p. 331.

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\* Weber has recently published a full bibliography of this disease (*Quart. Journ. Medicine*, vol. ii., 1908, p. 85) which renders any extensive reference to the literature unnecessary.

example, it is found, after the administration of 100 c.c. of carbon monoxide, that 20 per cent. of the hæmoglobin is combined with CO, it follows that 500 c.c. would have saturated all the hæmoglobin, or, in other words, that the total oxygen capacity of the hæmoglobin of the subject was 500 c.c., corresponding to about 370 grammes of hæmoglobin. If at the same time the percentage oxygen capacity of the blood be determined, the volume of the blood is readily ascertained. The capacity of the blood for oxygen per 100 c.c. is obtained by a simple hæmoglobinometer determination with the Haldane-Gowers instrument;<sup>2</sup> 100 degrees on the graduated tube correspond to an oxygen capacity of 18·5 c.c. oxygen per 100 c.c. of blood. If, for example, the blood in the example already mentioned required diluting to the mark 108 till it was equal in tint to the standard, the percentage oxygen capacity would be  $\frac{108 \times 18.5}{100} = 20$  c.c.; the volume of the blood, therefore, is  $\frac{500 \times 100}{20} = 2,500$  c.c. Some allowance has to be made for such hæmoglobin as is not in the circulating blood which is saturated with the carbon monoxide; it is not certain how much this is in man, but a full deduction is made if the calculated blood volume be reduced by 10 per cent.

On applying this method to the study of cases of disease in man, it appeared at once that anæmias might be real or apparent.<sup>3</sup> Pernicious anæmia on the one hand proved to be a real anæmia in which the total amount of hæmoglobin is in serious defect, though in most cases to a less degree than is indicated by the hæmoglobinometer owing to some increase in the volume of the blood. On the other hand, it turned out that in chlorosis and *Ankylostoma* anæmia<sup>4</sup> there is no material deficiency in the total amount of hæmoglobin, but that the low percentage oxygen capacity observed in the hæmoglobinometer is due to a great increase in the volume of the plasma. As far as chlorosis is concerned, these fundamental observations of

<sup>2</sup> Journal of Physiology, vol. xxvi., 1901, p. 497.

<sup>3</sup> Lorrain Smith, Trans. Path. Soc., London, vol. li., 1900, p. 311.

<sup>4</sup> Boycott and Haldane, Journal of Hygiene, vol. iii., 1903, p. 112.

Lorrain Smith have recently been confirmed by Plesch<sup>5</sup> and Oerum.<sup>6</sup>

This information as to the essential nature of the different varieties of anæmia is obviously of the very highest importance. Criticism of the results must be criticism of the method. We have recently made a number of observations on rabbits to determine by direct experiment whether the method gives reliable results. In the first place, animals in which the total hæmoglobin had been determined by the CO method were bled or transfused to known amounts, and the result of a subsequent CO determination compared with the calculated value. The results were as follows:—

Total hæmoglobin before: grms.	Hæmoglobin removed or added: grms.	Hæmoglobin after: grms.		
		Calculated.	Found.	Difference.
11·9	—4·25	7·65	7·5	—0·15
19·9	—4·9	15·0	13·9	—1·1
12·5	—5·15	7·35	7·8	+0·45
16·0	—4·4 /	11·6	11·5	—0·1
9·7	—3·6	6·1	6·5	+0·4
15·9	+4·55	20·45	20·7	+0·25
16·8	+4·85	21·65	21·2	—0·45
19·4	+5·25	24·65	24·2	—0·45

These figures show that the method gives consistent results. In the next series, animals whose total hæmoglobin had been determined by the CO method were bled to death, their vessels washed out, the carcass minced up, and all the hæmoglobin in the body collected and determined directly (Welcker's method). The mean result in a series of twelve animals was that the carbonic oxide method was 2 per cent. higher than the direct method—a satisfactory correspondence.

The Haldane-Lorrain Smith method, the accuracy of which is thus demonstrated, has thrown considerable light on some cases of polycythæmia, though much more work requires to be done with its aid before we can hope to get to the bottom of many of the problems in hand.

<sup>5</sup> Wiener Med. Wochenschr., vol. lvii., p. 1689.

<sup>6</sup> Deut. Arch. f. Klin. Med., vol. xciii., 1908, p. 357.

Since the derivation of words is wholly immaterial in this regard, we may say that by polycythæmia we mean a condition in which the hæmoglobin of the blood is more concentrated than usual. This increase of hæmoglobin is always, as far as we know, associated with an increase in the number of red cells per unit volume. There is, however, no reason why it should not be brought about by an increase in the size or density of the red corpuscles, their numbers remaining constant, and the blood may relatively frequently contain too many cells, without an excess of hæmoglobin.

Polycythæmia may indicate a real increase in the total hæmoglobin in the body, or a diminution in the volume of the blood. Concentration of the blood in this way is most familiar in the new-born and in conditions where there is a great loss of fluid from the body, as in severe diarrhœa and some acute infective conditions. Any substantial degree of concentration is not, however, easily brought about; the tendency of the blood to keep its volume constant at the expense, if necessary, of the tissue fluids is only overcome in states of extreme dehydration.

Polycythæmia indicative of a real increase in the total hæmoglobin is found in conditions where the body is exposed to chronic oxygen starvation. The increase in the number of red cells and the hæmoglobin percentage at high altitudes has been long known. The final result of a great number of conflicting experiments is that the increase is at first brought about by a concentration of the blood: later on, however, the volume of the blood is restored without reducing the oxygen-carrying power per unit volume by a real hypertrophy of hæmoglobin. In cases of congenital cardiac disease very considerable degrees of polycythæmia are often found. In view of the relatively slight symptoms of oxygen starvation which such cases may show, and considering the results obtained by Lorrain Smith,<sup>7</sup> in a case of adherent pericardium, there can be little doubt that we have here also a real increase in the total amount of hæmoglobin in the body. In many cases of acquired cardiac disease the same thing

<sup>7</sup> Trans. Path. Soc., London, vol. liii., 1902, p. 136.

probably occurs, though it may be obscured by an increase in the volume of the blood, so that the percentage oxygen capacity remains about normal. If the circulatory difficulties of cardiac disease result in a dilution of the blood in the early stages, this increased volume may be compensated by an increase in the total hæmoglobin, so that the oxygen-carrying power of each 100 c.c. of blood passing through the lungs is not very much diminished. For in such cases the increased rate of circulation, which is the compensatory mechanism for the diluted blood in chlorosis, is not available owing to the derangement of the pumping mechanism. The object of compensation is to send the right number of grammes of hæmoglobin through the lungs every minute; if the circulation is defective this can only be effected by increasing the percentage oxygen capacity of the blood.

A rise in the hæmoglobin content of the blood is produced by keeping animals in a chronic state of slight poisoning with carbon-monoxide, coal gas being added to the air in such concentration as will keep the hæmoglobin about 25 per cent. saturated with CO. The experiments of Nasmith and Graham<sup>8</sup> show that the change is of quite slow onset, so that there are grounds for believing that it is due to a real increase in the total amount of hæmoglobin.

The polycythæmia of *idiopathic splenomegalic polycythæmia* is of quite a different kind. In this interesting disease there is not only a considerable rise in the percentage oxygen capacity of the blood, but the volume of the blood is also increased, so that the total oxygen capacity is very much greater than normal. In this way an average case may have about a kilogram of hæmoglobin instead of 300—400 gms., and an extreme case as much as 2½ kilograms. By the kindness of Dr. Hutchison, Dr. Thompson, and Dr. Greenwood, we have been able to examine the total oxygen capacity and the blood volume by the CO method in three cases. The results are shown in the next table (cases 2, 3, 4) to which we have added the figures already published by Weber<sup>9</sup> (case 1).

<sup>8</sup> *Journal of Physiology*, vol. xxxv., 1906, p. 32.

<sup>9</sup> *Medico-Chirurgical Transactions*, vol. lxxxviii., 1905.

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	Sex.	Age.	Date.	Hæmoglobin per cent.	Total O <sub>2</sub> capacity c.c.	Blood volume c.c.	Per 100 grms. body weight.	
							c.c. O <sub>2</sub> capacity.	c.c. blood.
Case 1...	F	37	Nov. 30	156	1610	5600	2.4	8.2
			Jan. 21	148	1810	6000	2.7	9.7
Case 2...	M	38	Feb. 1	173	1620	4970	2.7	8.3
			Feb. 15	169	1480	4765	2.4	7.9
Case 3...	M	43	Feb. 1	176	3375	10,750	5.0	16.0
Case 4...	M.	53	June 30	155	1820	6330	3.0	10.4
Normal	...	...	...	...	...	...	0.85	5.0

The sequence of events in these cases seems pretty clear. There is first a great increase in the production of red cells; since the blood would become solid if the percentage hæmoglobin were about doubled, a secondary increase in blood volume takes place in order that the blood may be able to get round the body at all, and a state of true plethora is produced. Any considerable increase in blood volume introduces circulatory difficulties. The point, therefore, at which the concentration of hæmoglobin settles down—apparently about 150 per cent. on the scale—is decided by the balance of the disadvantages of too much blood on the one hand and too great a viscosity on the other. If the increase in blood volume were the primary fault—as, *e.g.*, in chlorosis—the percentage oxygen capacity would not rise beyond a normal level.

This accumulation of hæmoglobin in the body might be due to increased production or deficient destruction. Of the latter there is no evidence, though the pigmentation of fæces and urine is about all one has to judge by. There is, on the other hand, definite evidence in the blood of activity of the erythroblastic tissues. The red corpuscles may be somewhat variable in size, tending to be too small, the colour index low (0.6 to 0.8) and a few normoblasts may be present. Such nucleated red cells as are found are real normal normoblasts, without any polychromatophilia of the cytoplasm. Furthermore, an excessive proportion of neutrophile, eosinophiles and basophile leucocytes may indicate an associated activity of the leucoblastic apparatus. These findings are confirmed by the isolated post-mortem examinations

which have been made.<sup>10</sup> It is pretty clear, therefore, that the excess of hæmoglobin is due to over-production.

This overgrowth of red cells might occur in response to some stimulus—on the one hand, lack of oxygen, either because the tissues want more than usual, or because the hæmoglobin can carry an unnaturally small amount per unit weight, or, on the other hand, excessive blood destruction. The extreme and sustained degree of response is against this latter hypothesis, and there is no positive evidence at all either of deficiency of oxygen or of too much blood destruction. The overgrowth of red cells is indeed not to be regarded as a rational hypertrophy of a definite character and degree, and in response to a definite stimulus, but as a neoplastic formation of a benign character, meaningless in origin and purposeless in character. Like other benign new growths, it causes ill-effects mechanically, the heart eventually giving way under the strain of the viscosity of the blood. A solid tumour of red cells is extremely rare; such has, however, been described under the name of “erythrocytoma,” an otherwise appropriate name for the present condition. The fluid and solid tumours of leucoblastic tissue afford an obvious parallel in lymphatic leuchæmia and some of the infiltrating lymphomata.

The early stages of splenomegalic polycythæmia have not yet been identified. There appear, however, to be some individuals, who cannot be described as otherwise than normal in all other respects, who have too much hæmoglobin. One such case we have twice examined by the CO method with the following results:—

Date.	Hæmoglobin per cent.	Total O <sub>2</sub> capacity c.c.	Blood volume c.c.	Per 100 grms. body weight.	
				c.c. O <sub>2</sub> capacity.	c.c. blood.
June 30 ...	107	1050	5300	1·47	7·4
July 6 ...	106	1000	5100	1·40	7·1
Normal ...	100	600	3250	0·74–0·95	4·2–6·3

<sup>10</sup> Clinical Society's Transactions, vol. xxxviii., 1904; *Lancet*, March 17th, 1906.



Oerum<sup>11</sup> has also recently described a normal man with 8·3 c.c. blood and about 1·5 c.c. oxygen capacity per 100 grammes body weight.

The symptoms from which these cases suffer seem to be due in the main to the increased viscosity of the blood. The rational treatment, therefore, is to bleed them very freely and very frequently. This will reduce the viscosity, though the volume will probably remain much the same. There is no danger that the bleeding will excite the bone marrow to further activity; regeneration after bleeding is a response to deficiency of hæmoglobin, not to loss of blood.

<sup>11</sup> *Loc. cit.*

# SOME OBSERVATIONS ON ARTERIAL BLOOD-PRESSURE IN HEALTH AND DISEASE.

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By

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THERE appeared in the *Lancet* of September 8th, 1906, a paper from the pen of Dr. H. Starling, in which evidence was brought forward to show that in ordinary cases of cardiac failure, resulting from valvular disease, the "systolic blood-pressure," as registered by the manometer, was invariably higher than is normal in healthy individuals. In support of such opinion, reference was made to the enormous reserve power of the cardiac mechanism as displayed by the classical experiment of Cohnheim with the aortic ligature, where the arterial blood-pressure was found to rise in the peripheral vessels in spite of the increasing resistance offered in the first part of the aorta to the ventricular output.

So many clinical facts, however, of every-day occurrence, are explained on the assumption that, in cases of "failing heart," there is a steady fall in the arterial blood-pressure, that I have considered the subject deserving of further observations.

Attention was first directed to an estimation of the arterial blood-pressure, and its daily variations in healthy individuals, as a result of the ordinary incidents and accidents of everyday life.

The instrument used for making these observations was Martin's modification of the Riva-Rocci manometer. It consists simply of a manometer, connected by means of a stout rubber tube with a collapsible rubber bag, oblong in shape, which is fastened to the arm of the patient by means of two straps. A "T" piece, provided with an escape valve, connects the tubing with a simple air-pump, so that the bag can be filled with air under pressure, or emptied, at will. The bag is made of two thicknesses of gutta-percha—the inner, thin, which is in contact with the arm, is very elastic; the outer is non-distensible.

If a normal individual be taken, and if the bag, previously strapped to the arm, be gradually distended with air, it will be found that at a certain level of mercurial pressure, which varies in different individuals, the radial pulse is lost. This reading will give the maximum systolic pressure in millimetres of mercury. If, now, the air in the bag be allowed to escape slowly, the observer will notice that, with the falling pressure, the pulse waves will reappear, quite suddenly, at a reading slightly lower on the scale than that which he previously registered, but which latter reading is constant. This is the mean pressure of the ventricular systole in the brachial artery. He will, however, notice that, *at this reading*, the *full* pulse wave is not obtained at the wrist, though every beat can be felt. As, however, a further amount of air is allowed to escape from the bag, there will come a time when he will appreciate a sudden change in the character of the wave impinging against the finger, the full characteristics of the individual's pulse will be felt with the normal excursion of the arterial wall. The third reading corresponds to the mean diastolic pressure in the vessel.

The difference between these two latter readings, the mean systolic and the mean diastolic pressure, as also the actual value of them, varies much at different ages, in different individuals, in health and disease, with rest and exercise. Apparently, in most healthy individuals, the difference between the two readings measures about thirty millimetres of mercury. The variations which occur as the result of disease will be mentioned hereafter. The observer will not, however, fail to notice that even in health, at different hours of the day, he will obtain different readings, and at the end of this paper, figures are given recording a number of observations made upon different individuals, apparently quite healthy, who were leading useful and active lives. It may here be stated that there seems to be no doubt that the blood-pressure, as registered by this manometer in the manner above described, is *lowest* immediately on waking, before rising or moving, in the morning, and rises during the day until about six o'clock. This rise is noticed not only in the case of the mean diastolic pressure, but also in the case of the mean systolic pressure. The rise,

however, of the former is greater than the rise of the latter. Later in the evening, both readings of blood-pressure will be bound to be falling again. As a result of vigorous exercise, there is a marked rise noticed in the value of both systolic and diastolic pressure. The exercise taken, swimming, running, playing "squash" racquets, physical drill, produced greater or less variations according to the time of day at which it was taken, and according to the "condition" of the individual, that is to say, whether "trained" or "untrained." For instance, in the early morning, immediately on rising, the effect of exercise stimulates the heart to rather excitable action, so that it beats very vigorously, possibly more vigorously than is necessary. And it will also be noticed that, as in cases of failing heart hereafter mentioned, some of the ventricular beats are much more forcible than others, so that a maximum systolic reading is obtained, possibly some 20 mm. above the mean systolic pressure, and only occurring, perhaps, once in twelve or twenty beats. Later in the day this tendency to excitable action is by no means so marked; possibly the vaso-motor mechanism is more alive and ready to appreciate changes occurring in the action of the central cardiac mechanism as the result of environment. The observer will also notice this tendency to excitable action—and therefore to abnormal increase in blood-pressure—in individuals who are totally "untrained" or imperfectly "trained." I am inclined to think that it will also be found in individuals who are "overtrained," that is to say, "stale." It will be noticed that there is a retardation or slowness exhibited in the rise of the mean diastolic pressure in such people after any given amount of exercise, although a maximum systolic reading has appeared which has disturbed the normal relationship between systolic and diastolic pressure.

Another series of observations were taken in the cases of healthy people who had taken vigorous exercise shortly after taking a substantial meal, that is to say, while the splanchnic area was in a state of general vaso-dilatation. The diastolic pressure remained low—in one case it was lower than normal; the mean systolic pressure was considerably higher than normal,

but the wave coming through at this reading was small, and it was evident that the pressure recorded only existed for a very short portion of the cardiac systole. Irregular beats were also felt, occurring at considerable intervals, and due apparently to excitable cardiac action (max. syst. press.).

This tendency, however, to excitable action (the rhythm remaining regular) is not shown in the case of individuals who are in "training." In such people the mean systolic pressure never rises to so great an extent, but the diastolic pressure rises early and remains above normal for some time. Irregular maximum systolic readings are absent. The phenomenon known as "second-wind," which occurs in the case of a runner who is imperfectly trained, is associated apparently with the facts detailed above. While the man is distressed, and *before* he obtains relief with the advent of "second-wind," mean diastolic pressure remains low, recovering and rising with the disappearance of his distress, the mean systolic pressure having risen earlier and remained constant.

Transient rises in the mean systolic pressure have been noticed after such incidents as vomiting, coughing, and straining at stool; the increase in pressure varied with the degree of trouble, but it was of short duration.

From a consideration of the facts recorded above, it will be obvious that, even in healthy individuals, considerable variation in arterial blood-pressure occurs, both as regards the actual value of systolic and diastolic pressure, and as regards the relation which these two values bear to one another.

#### BLOOD-PRESSURE READINGS FROM HEALTHY PEOPLE.

TABLE I.—Ten readings taken morning (7 a.m.), and evening (5 p.m.), on ten successive days. Male. Age 28. Figures refer to millimetres of mercury.

	Morning.			Evening.	
	Diastolic.	Systolic		Diastolic.	Systolic.
1	94	120		110	130
2	90	120		106	126
3	92	122		110	140
4	94	120		108	136
5	94	120		112	140
6	96	122		112	138
7	94	120		108	136
8	92	120		110	136
9	92	120		110	138
0	94	120		110	140

The morning readings were taken before rising, while the individual was in bed. The evening readings, in each case, after a moderate and variable amount of exercise. The actual value of the reading varies in different individuals. I have found diastolic pressure to vary between 84 and 120, and systolic pressure between 116 and 150, under conditions which were apparently similar. The general rise in blood-pressure, morning to evening, as above, is apparently the rule.

TABLE II.—Readings taken to show the effect of exercise upon arterial blood-pressure. The figures represent the mean values of a number of records in millimetres of mercury.

	Morning on waking.	After exercise. Time, 8 a.m.	Mid-day.	After exercise.	Evening.
1.					
Diastolic ...	90	100	100	100	110
Systolic ...	120	150	130	150	130
Max. Systolic ...	—	—	—	160 ( $\frac{1}{10}$ )*	—
2.					
Diastolic ...	90	—	104	110†	108
Systolic ...	122	—	130	140	130
Max. Systolic ...	—	—	—	—	—
3.					
Diastolic ...	85	90	95	—	96
Systolic ...	110	130	120	—	120
Max. Systolic ...	—	—	—	—	—
4.					
Diastolic ...	94	—	96	94	100
Systolic ...	120	—	126	144	132
Max. Systolic ...	—	—	—	170 ( $\frac{1}{10}$ )‡	—
5.					
Diastolic ...	92	—	—	120	110
Systolic ...	126	—	—	160	140
Max. Systolic ...	—	—	—	—	—
6.					
Diastolic ...	88	88	100	—	106
Systolic ...	120	136	128	—	130
Max. Systolic ...	—	—	—	—	—

\* Violent exercise taken about half an hour after a meal. Heart somewhat excitable in action; one beat in ten.

† Time—4 p.m. exercise.

‡ Exercise shortly after a meal.

TABLE III.—Readings taken to show the variation in blood-pressure observed, as a result of exercise, in the case of individuals in “training” or in want of “training.”

	Usual daily variation.	After exercise “untrained.”		After exercise “in training.”
1.				
Diastolic ...	96 to 110	100	—	130
Systolic ...	124 to 130	170	—	160
Max. Systolic ...	—	180 ( $\frac{1}{15}$ )†	—	—
2.				
Diastolic ...	92 to 114	118 to 120	134*	132
Systolic ...	126 to 138	158	160	160
Max. Systolic ...	—	170 ( $\frac{1}{15}$ )	—	—
3.				
Diastolic ...	88 to 94	110	124*	120
Systolic ...	114 to 122	146	150	144
Max. Systolic ...	—	158 ( $\frac{1}{5}$ )	—	—
4.				
Diastolic ...	100 to 108	114	130*	123
Systolic ...	124 to 134	152	160	158
Max. Systolic ...	—	162	—	—
5.				
Diastolic ...	94 to 98	102	—	116
Systolic ...	120 to 124	150	—	146
Max. Systolic ...	—	—	—	—

\* These readings taken after “second-wind.”

† One beat in fifteen.

The above figures were taken from five different individuals, and represent the mean value of a large number of observations.

### HEART DISEASE.

Two hundred cases of cardiac disorder admitted into the wards were examined. The majority of these were suffering from symptoms which were indicative of dilatation of the organ; the extent of the disease, valvular and myocardial, was variable, but in most cases it was advanced. For some time after admission records were taken, in many cases four or five times daily, both before and after the exhibition of drugs, and note was taken of any other complications, such as vomiting or coughing, which might tend to produce such changes as occur in normal individuals. From a consideration of the figures recorded we are of opinion that in all cases of “failing heart,” the result of either myocardial or valvular trouble, the main diastolic pressure

steadily falls, and falls below normal, very rapidly in cases of acute dilatation and where a last fight for life is being made. With regard to systolic pressure, it is very characteristic of all cases of failing heart that individual cardiac beats have a different value, quite apart from any irregularity as regards rhythm and rate. Taking a typical case—after inflating the bag until the pulse had disappeared, it was found that one wave beat in fifteen heart beats appeared at the wrist at a pressure of 165 mm., the volume of the wave was very small. When the pressure registered 150 mm., three pulse waves, still very small, came through out of a dozen heart beats. At a pressure of 145 mm. six out of twelve beats were felt. At times there was an irregular kick of the left ventricle, occurring apparently as an extra systole, which reached as high a figure as 168 mm. Every heart beat was felt at the wrist when the pressure in the bag registered 135 mm., but the waves so appearing were much smaller than those felt at the same time in the opposite wrist (the two pulses were equal in reality), and the full wave was not appreciated by the finger until the pressure in the bag registered 78 mm. As the patient's general condition improved, the irregular readings and maximum systolic pressure disappeared; there was a marked rise in diastolic pressure: 78 mm. to 96 mm. The mean systolic pressure first of all rose somewhat, and then subsequently fell to 130 mm. These changes occurred as a result of rest with medicinal and dietetic treatment. The readings taken in the afternoon were all of them invariably higher than those recorded in the morning, unless there had been some grave change in the patient's condition, thus exhibiting the same tendency to variation which, as has been mentioned above, occur normally in healthy active people. An evening reading taken immediately after the patient had been allowed to get up for the first time showed some rise in the value of the mean systolic pressure, which rise was smaller as improvement in general health was maintained. The diastolic pressure in this case did not show any alteration in value, but not at all infrequently we have observed a fall, and it is our opinion that if a fall in diastolic pressure is observed in such cases, then the patient has been allowed to get up too soon, and



more prudent counsels must prevail. In one case which I can recall, but of which I have unfortunately lost the actual figures, the patient had been permitted to get up three times, and on each evening a fall in diastolic pressure had been noted. On the fourth night, she had an attack of acute cardiac dilatation and died.

The actual height of the systolic pressure, as measured by the manometer, depends a good deal upon the presence or absence of left ventricular hypertrophy. Thus in long-standing cases of mitral regurgitation, accompanied by considerable hypertrophy, the reading obtained is considerably higher than the highest readings found in healthy people, but the pressure is only sustained for a very small part of the cardiac systole, and the wave felt is only a small one. In some cases of aortic regurgitation, accompanied by tremendous ventricular hypertrophy, the wave may be felt at the wrist when the pressure measures 190 mm. of mercury; but such pressure is not sustained, it is irregular in value, and consequently of little benefit to the individual, whom it endows with a throbbing headache. Mean diastolic blood-pressure, however, is very low, and I have found it varying from 68 mm. to 100 mm. It is in cases of aortic regurgitation that the greatest extreme is noticed between mean systolic and mean diastolic pressure. In some of my earlier estimations I was inclined to think that, with such a high systolic reading, the aortic incompetence was secondary to renal insufficiency with chronic interstitial nephritis, but this was due to a failure to recognise the low value of the diastolic pressure, and was disproved at the autopsy. A number of my earlier records are valueless for this reason, and are not here recorded (Tables XVII., XIX., XX., XXI.).

I have noticed that the appearance of the presystolic bruit in cases of mitral stenosis, which is taken to indicate recovery of and increased power of contraction in the left auricular wall, is always accompanied by a rise in the mean diastolic pressure, and until the mitral mid-diastolic bruit of the failing heart gives place to the mitral presystolic bruit, such improvement does not take place (Table V.).

A very rapid fall in the value of the diastolic pressure accompanies pericardial effusion. A fall in the systolic pressure is not at first noticeable, owing to the sharp short "kicking" of the left ventricle giving irregular readings of 160 mm., 170 mm., or 180 mm. (Table VI.).

With the knowledge of the gravity of alcoholic myocardial degeneration, and of the fact that in these cases of "drinker's heart" the interval between the appearance of œdema and the departure to the post-mortem room is only some eight weeks, it would naturally be expected that blood-pressure would be low. In the few cases which I have been able to examine I have found both diastolic and systolic pressures to be of low value, and I have not noticed the same tendency to high, short, irregular systolic "kicking," which is characteristic of failing valvular cases. It would seem that the drinker's heart exhibits little or no tendency to recovery, but a progressive fall of blood-pressure in the arterial system (Table XIV.).

One case (Table XVI.) which I examined was interesting on account of the fact that an exceedingly high blood-pressure gave rise to a diagnosis of interstitial nephritis. At the autopsy a very dilated and hypertrophied heart was found, with "cardiac" kidneys. There was history of alcoholic excess for years past. This may possibly have been an example of the "beer-drinker's" heart, described by Dr. Hale White, in a previous number of the *Guy's Hospital Reports*, in which type of cardiac disorder there is to be found hypertrophy without any microscopical evidence of myocardial degeneration.

The extreme value of venesection in cases of advanced mitral failure, in which condition drugs seem powerless to influence cardiac action, is so generally recognised that a fair number of readings were taken before and after its performance, and, in some cases, during the operation. The amount of blood removed, in every case from the arm, varied, but with those cases in which the quantity of blood removed was eight ounces or under, there was practically no change noticed in either systolic or diastolic pressure. All the patients were adults. When the quantity of blood removed was ten ounces or over (up

to twenty-three ounces) the immediate effect of the venesection was a rise in the mean systolic blood-pressure, a marked steady-ing of the heart's action with a disappearance of irregular maximum systolic readings. At first there was practically no change in the mean diastolic arterial pressure; in about four hours' time a rise was noticed in all cases (Tables VIII. and IX.).

### BLOOD-PRESSURE READINGS IN HEART DISEASE.

TABLE IV.—Case of mitral regurgitation. Woman. Age 23. Admitted for œdema and breathlessness. Rheumatic history. First attack when 16. Organic disease diagnosed two years previously to admission. Readings taken night and morning on ten successive days. Figures refer to millimetres of mercury.

				Diastolic.	Systolic.	Max. Systolic.
1	5.0 p.m.	...	...	84	110	140 ( $\frac{1}{8}$ )*
2	9.45 a.m.	...	...	84	106	150 ( $\frac{1}{8}$ )
	6.0 p.m.	...	...	90	120	
3	10.15 a.m.	...	...	92	120	
	5.30 p.m.	...	...	96	122	
4	12 noon	...	...	88	122	140 ( $\frac{1}{10}$ )
	7.0 p.m.	...	...	90	122	
5	10.0 a.m.	...	...	94	124	
	5.0 p.m.	...	...	96	124	
6	10.15 a.m.	...	...	96	124	
	5.40 p.m.	...	...	96	128	
7	9.45 a.m.	...	...	98	130	
	7.0 p.m.	...	...	96	126	
8	10.15 a.m.	...	...	96	126	
	6.0 p.m.	...	...	98	128	
9	12.30 p.m.	...	...	98	130	
10	5.15 p.m.	...	...	98	130	

\* One beat in six.

The patient was discharged after three weeks. Heart compensated. Treatment by digitalis. Rest.

TABLE V.—Case of mitral stenosis and regurgitation. Dilation. Has been liable to heart trouble for seven years. Female. Age 33. Œdema. Bronchitis. Dyspnoea.

	Diastolic.	Systolic.	Max. Systolic.
1 On admission ... ..	86	110	150 ( $\frac{1}{2}$ )
2 After a bad night. Some sickness	84	108	148 ( $\frac{1}{2}$ )
Evening reading ... ..	84	110	148 ( $\frac{1}{2}$ )
3 Third day ... ..	84	112	148 ( $\frac{1}{2}$ )
4 Fourth day ... ..	86	114	148 ( $\frac{1}{2}$ )
5 Sixth day. Morning	86	120	140 ( $\frac{1}{2}$ )
Evening*	90	122	140 ( $\frac{1}{2}$ )
6 Seventh day. Morning	92	126	
Evening†	96	126	144 ( $\frac{1}{2}$ )
7 Ninth day ... ..	96	130	
8 Tenth day ... ..	96	128	
From this time she steadily improved			
9 Seventeenth day ... ..	94	128	

\* Presystolic bruit first heard replacing mid-diastolic bruit occasionally.

† Presystolic bruit constant. Œdema clearing up.

TABLE VI.—To show the effect of pericardial effusion. Female. Age 19. Aortic regurgitation with mitral stenosis.

	Diastolic.	Systolic.	Max. Systolic.
1 Three hours after admission ...	90	126	160 ( $\frac{1}{2}$ )
2 Second day ... ..	94	128	154
3 Third day ... ..	92	128	156
4 Fourth day. Pericardial rub heard	94	?	?
5 Fifth day. Signs of pericardial effusion	84	110	160 ( $\frac{1}{2}$ )
6 Sixth day. Morning	84	108	158 ( $\frac{1}{2}$ )
Evening	82	100	160 ( $\frac{1}{2}$ )
7 Seventh day. Dying. No reading.			

TABLE VII.—Fireman, railway. Age 28. Mitral regurgitation with hypertrophied left ventricle. No œdema. Dyspnœa. Palpitation.

	Diastolic.	Systolic.	Max. Systolic.
1 Shortly after admission ...	86	130	
2 ... ..	90	134	
3 ... ..	90	132	
4 ... ..	88	138	
5 ... ..	90	140	
6 ... ..	90	138	
7 ... ..	90	140	
8 After getting up first time. Evening reading	84	120	150 ( $\frac{1}{2}$ )
9 Staying in bed. Not so well	88	134	
10 A week later ... ..	94	134	
Subsequent improvement.			

TABLE VIII.—Mitral stenosis. Seven years' standing. Bronchitis. Right-sided dilatation. Venesection (sixteen ounces) at 10 p.m. first night. Male. Age 33.

	Diastolic.	Systolic.	Max. Systolic.
1 On admission—			
5.0 p.m. ...	80	100	160 ( $\frac{1}{2}$ )
8.0 p.m. ...	80	98	170 ( $\frac{1}{2}$ )
11.0 p.m. ...	82	120	150 ( $\frac{1}{2}$ )
2 Second day—			
8.0 a.m. ...	86	120	
12.30 p.m. ...	88	120	
4.0 p.m. ...	88	120	
10.0 p.m. ...	90	124	
3 Third day—			
10.0 a.m. ...	90	124	
4.30 p.m. ...	92	126	
4 Fourth day—			
10.15 a.m. ...	92	126	
5.30 p.m. ...	90	126	
5 Fifth day. Evening	94	124	
6 Sixth day. Evening	96	126	
7 Tenth day. Evening	94	126	
8 Eleventh day—			
Morning	90	130	
Evening	96	128	
9 Twelfth day—			
Evening	96	128	
Subsequently did well.			

TABLE IX.—To illustrate effect of venesection. Male. Age 26. Mitral stenosis. Right-sided failure.

	Diastolic.	Systolic.	Max. Systolic.
1 Before venesection ..	84	104	150 ( $\frac{1}{2}$ )
2 After venesection (18 ounces)—			
Half an hour later	84	122	
Two hours later	84	126	148 ( $\frac{1}{2}$ )
Four hours later	92	128	
Fifteen hours later	96	128	
3 Next day ...	96	126	

TABLE X.—Boy. Age 9 $\frac{1}{2}$ . Scarletina at the age of 4 $\frac{1}{2}$ . Endocarditis; mitral regurgitation with dilated heart; diagnosed in February, 1902. He has been admitted since that time, two or three times every year. In October, 1903, mitral stenosis was diagnosed. During the past year he has been in hospital almost continuously. Cardiac dilatation and adherent pericardium.

			Diastolic.	Mean Systolic.	Max. Systolic.
1906					
November 7	6.30 p.m. ...	?		92 mm.	110 mm. ( $\frac{1}{2}$ )
	8.45 p.m. ...	?		92	110 mm. ( $\frac{1}{2}$ )
November 8	10.15 a.m. ...	?		100	110( $\frac{1}{2}$ )-130( $\frac{1}{10}$ ) mm.
	8.45 p.m. ...	—		100	110( $\frac{1}{2}$ )-140( $\frac{1}{10}$ ) mm.
November 9	10.5 a.m. ...	—		100	126( $\frac{1}{2}$ ) mm.
November 12	10.30 a.m. ...	—		100	118( $\frac{1}{2}$ )-128( $\frac{1}{12}$ ) mm.
	6.30 p.m. ...	—		100	118( $\frac{1}{2}$ )-128( $\frac{1}{12}$ ) mm.
November 13	Evening ...	—		110	120( $\frac{1}{2}$ )-144( $\frac{1}{16}$ ) mm.
November 16	Evening ...	98		120	150( $\frac{1}{12}$ ) mm.
November 19	Evening ...	98		120	142( $\frac{1}{12}$ ) mm.
November 21	Evening ...	?		100	118( $\frac{1}{2}$ )-130( $\frac{1}{10}$ ) mm.
November 23	Evening ...	?	} Very irregular		{ 120-160( $\frac{1}{16}$ )
November 24	Evening ...	?			

Final stage, cardiac sickness.

TABLE XI.—Female. Age 70. Mitral regurgitation, following rheumatic fever at the age of 25. Compensation for many years. Arterio sclerosis. Cardiac dilatation. Admitted with urgent dyspnoea and rapid heart's action.

			Mean Systolic.	Max. Systolic.
1906				
November 1	12.15 p.m. ...	...	120 mm.	140 ( $\frac{1}{8}$ )
	3.30 p.m. ...	...	122	140 ( $\frac{1}{8}$ )
	9.15 p.m. ...	...	130	140 ( $\frac{1}{8}$ )
	9.20 p.m.*	...	160	
	9.30 p.m. ...	...	160	172 mm. ( $\frac{1}{10}$ )
	9.40 p.m. ...	...	156	
	11.15 p.m. ...	...	154	
November 2	10.45 a.m. ...	...	154	
November 3	2.0 p.m. ...	...	154	
	6.30 p.m. ...	...	160	Coughing
November 4	12.30 p.m. ...	...	150	
	7.50 p.m. ...	...	154	
November 5	6.30 p.m. ...	...	150	
November 6	12.40 p.m. ...	...	148	
	6.0 p.m. ...	...	148	
November 7	10.30 p.m. ...	...	148	
	6.20 p.m. ...	...	150	
November 8	10.30 a.m. ...	...	148	
	6.15 p.m. ...	...	150	
November 9	10.20 a.m. ...	...	146	
November 13	10.30 a.m. ...	...	148	
November 14	5.30 p.m. ...	...	148	
November 15	6.45 p.m. ...	...	150	
November 16	10.25 a.m. ...	...	150	
November 17	5.30 p.m. ..	...	148	
November 19	10.30 a.m. ...	...	154	
	3.55 p.m. ...	...	148	
November 23	3.0 p.m. ...	...	150	
November 24	6.0 p.m. ...	...	148	
November 25	12.40 p.m. ...	...	150	

\* Strychnine injected. Eight minims at 9.15 p.m.

There was no variation noticed further. She was discharged about the end of December. Compensation established.

TABLE XII.—Female. Age 22. Valvular disease of five years' standing. Mitral regurgitation. Œdema.

				Diastolic.	Systolic.	
1906						
November 21	Evening	...		90 mm.	118 mm.	
November 23	Morning	...		90	124	
	Evening	...		90	130	
November 24	Evening	...		100	140	
November 25	Morning	...		98	136	
November 27	Evening	...		98	132	
December 1	Evening	...		90	128	
December 6	Evening	...		100	130	
1907						
January 1	Discharged	...		Same	reading.	

On readmission with similar symptoms.						Max. systolic.
February 5	...	...	90	126		140( $\frac{1}{8}$ ) mm.
February 6	...	...	88	128		148( $\frac{1}{8}$ ) mm.
February 7	...	...	92	130		
February 8	...	...	92	126		
February 9	...	...	94	126		132( $\frac{1}{8}$ ) mm.
February 10	...	...	96	124		130( $\frac{1}{8}$ ) mm.
February 11	...	...	100	130		
February 12	...	...	100	130		
February 13	...	...	100	130		
February 16	...	...	100	132		
February 21*	...	...	94	130		140( $\frac{1}{8}$ ) mm.
February 24	...	...	100	132		

\* This reading was taken after she had been allowed to get up for the first time.

She made a good recovery on both occasions, the œdema rapidly clearing up, with rest in bed, and the heart's action slowing under the influence of digitalis.

TABLE XIII.—Fatty degeneration of the heart. Cardiac dilatation. Mitral regurgitation. Alcoholism. Female. Age 49.

			Diastolic.	Mean Systolic.	Max. Systolic.
1906					
November 3	8.35 p.m.	...	88 mm.	104 mm.	186( $\frac{1}{2}$ ) mm.
November 4	12.20 p.m.	...	86	110	134( $\frac{1}{2}$ )
	8.5 p.m.	...	84	110	
November 5	10.30 a.m.	...	84	110	
	6.20 p.m.	...	86	115	
November 6	10.0 a.m.	...	90	114	
	12.35 p.m.	...	90	118	
	6.0 p.m.	...	92	116	
November 7	10.20 a.m.	...	90	116	
	6.15 p.m.	...	86	116	
November 8	10.20 a.m.	...	84	110	134 mm. ( $\frac{1}{2}$ )
	6.10 p.m.	...	86	110	
November 9	10.15 a.m.	...	84	122	
November 10	6.15 p.m.	...	86	130	138 mm. ( $\frac{1}{2}$ )
November 13	6.0 p.m.	...	86	124	150 mm. ( $\frac{1}{2}$ )

High irregular readings appeared four days before death. She died quite suddenly.

TABLE XIV.—Alcoholic myocarditis. Cirrhosis of the Liver. Male. Age 43. Death.

					Diastolic.	Systolic.	Max. Systolic.
1	Evening	...	...	...	80	100	120 ( $\frac{1}{2}$ )
2	Morning	...	...	...	78	98	
	Evening	...	...	...	76	96	
3	Morning	...	...	...	80	100	
	Evening	...	...	...	78	96	
4	Morning	...	...	...	76	96	

Died.

TABLE XV.—Fatty degeneration of heart. Female. Age 62. Death.

			Diastolic.	Systolic.	Max. Systolic.
1	6.15 p.m.	...	82	90	100 ( $\frac{1}{2}$ )
	9.30 p.m.	...	82	100	106 ( $\frac{1}{2}$ )
2	10.0 a.m.	...	80	100	106 ( $\frac{1}{2}$ )
	7.10 p.m.	...	86	100	106 ( $\frac{1}{2}$ )
3	6.50 p.m.	...	80	100	110 ( $\frac{1}{2}$ )
4	10.0 a.m.	...	?	92	...

Died in the evening.



TABLE XVI.—Female. Age 46. Cardiac dilatation, with tremendous hypertrophy of left ventricle. A mitral regurgitant bruit was heard at times. When first admitted there was considerable cedema. This cleared up slowly. She was discharged after six weeks in hospital, at her own request, with considerable relief. Readmitted three weeks later, under Dr. Taylor, and only lived about a week.

					Mean Systolic.	Max. Systolic.
1906						
November 12	10.10 a.m.	..	...	...	180 mm.	210 mm. ( $\frac{1}{2}$ )
	8.30 p.m.	...	...	...	195	
November 13	10.15 a.m.	...	...	...	200	
November 14	10.10 a.m.	...	...	...	200	
	4.55 p.m.	...	...	...	210	
November 16	2.25 p.m.	...	...	...	200	
	8.45 p.m.	...	...	...	200	
November 17	5.25 p.m.	...	...	...	200	
November 18	12.50 p.m.	...	...	...	200	
November 19	Morning	...	...	...	210	
November 20	Morning	...	...	...	208	
	Evening	...	...	...	210	
November 21	Evening	..	...	...	210	
November 22	Morning	...	...	...	202	
November 23	Morning	...	...	...	200	
November 24	Evening	...	...	...	190	
November 25	Evening	...	...	...	190	
November 26	...	...	...	...	190	
November 29	...	...	...	...	190	
November 30	...	...	...	...	192	
December 1	...	...	...	...	190	
December 3	...	...	...	...	192	
December 6	...	...	...	...	190	

On readmission, under Dr. Taylor, the following readings were taken on consecutive days:—

				1.	2.	3.
Diastolic	...	...	...	120	124	124
Mean Systolic	...	...	...	180	180	178
Max. Systolic	...	...	...	210 ( $\frac{1}{10}$ )	200 ( $\frac{1}{8}$ )	190 ( $\frac{1}{4}$ )

The case was of interest because of the fact that a diagnosis was made, on each admission, of chronic interstitial nephritis. At the autopsy a very hypertrophied and dilated heart was found. No evidence of old or recent endocarditis. The kidneys were *not* “granular,” but of the so-called “india-rubber,” or cardiac type. Possibly a case of “beer-drinker’s” heart.

TABLE XVII.—Aortic disease. Hypertrophy and dilatation of heart. Mitral incompetence. Œdema. Bronchitis. Anginal attacks. Daily readings. Male. Age 40.

					Diastolic.	Systolic.	Max. Systolic.
1	...	...	...	...	86	116	170 ( $\frac{1}{8}$ )
2	...	...	...	...	86	116	168 ( $\frac{1}{8}$ )
3	...	...	...	...	88	116	180 ( $\frac{1}{8}$ )
4	...	...	...	...	86	118	174 ( $\frac{1}{10}$ )
5	...	...	...	...	88	120	170 ( $\frac{1}{10}$ )
6*	...	...	...	...	88	110	184 ( $\frac{1}{8}$ )
7	...	...	...	...	88	120	170 ( $\frac{1}{8}$ )
8	...	...	...	...	86	122	160 ( $\frac{1}{8}$ )
9	...	...	...	...	90	120	164 ( $\frac{1}{8}$ )
10	...	...	...	...	88	124	160 ( $\frac{1}{8}$ )

\* Taken after an anginal attack. ? Dilatation of left ventricle. Note the high reading from the irregular "kicking" of the left ventricle.

TABLE XVIII.—Aortic stenosis. Cardiac dilatation. Angina pectoris. Vomiting. Female. Age 32.

					Mean Systolic.	Max. Systolic.
1906						
October	29	6.30 p.m.	...	...	92 mm.	110 ( $\frac{1}{8}$ )
		9.5 p.m.	...	...	90	
October	30	10.15 a.m.	...	...	92	
		2.15 p.m.	...	...	90	120 mm. ( $\frac{1}{8}$ )
		6.30 p.m.	...	...	90	
October	31	10.10 a.m.*	...	...	88	
		5.50 p.m.	...	...	95	120 mm. ( $\frac{1}{10}$ )
November	1	5.45 p.m.	...	...	92	
November	2	11.5 a.m.	...	...	98	
November	3	2.15 p.m.	...	...	92	122 mm. ( $\frac{1}{12}$ )
November	4	12.40 p.m.	...	...	94	
November	5	6.45 p.m.*	...	...	86	
November	6	12.40 p.m.*	...	...	88	110 ( $\frac{1}{10}$ )
		6.20 p.m.	...	...	90	
November	7	6.30 p.m.	...	...	94	
November	8	6.30 p.m.	...	...	100	110 ( $\frac{1}{10}$ )
November	11	2.55 p.m.	...	...	100	
November	24	6.20 p.m.	...	...	114	
November	27	3.40 p.m.	...	...	106	110 ( $\frac{1}{10}$ )
December	29	6.30 p.m.	...	...	120	
1907						
January	7	6.45 p.m.	...	...	120	110 ( $\frac{1}{10}$ )
January	16	2.55 p.m.*	...	...	92	

\* Taken shortly after anginal seizures.

TABLE XIX.—Aortic regurgitation. Mitral stenosis and regurgitation. Pericarditis. Male. Age 17. Heart very irregular in action. Death.

				Diastolic.	Mean Systolic.	Max. Systolic.
1906						
February 11	5.35 p.m.	...		90 mm.	138 mm.	146 mm. ( $\frac{1}{2}$ )
February 12	5.40 p.m.	...		90	138	146 mm. ( $\frac{1}{2}$ )
February 13	2.10 p.m.	...		84	136	146 mm. ( $\frac{1}{2}$ )
February 14	2.40 p.m.	...		90	128	Steady
February 16	5.0 p.m.	...		84	140	150 ( $\frac{1}{2}$ )
	8.30 p.m.	...		86	140	154 ( $\frac{1}{2}$ )

Died a few hours later.

TABLE XX.—Aortic regurgitation. Cardiac dilatation and hypertrophy. Male. Age 45.

				Systolic.	Max. Systolic.
1907					
November 5	Admission	12.10 p.m.		150 mm.	166 mm. ( $\frac{1}{2}$ )
	6.45 p.m.	...		140	146 mm. ( $\frac{1}{2}$ )
November 6	10.20 a.m.	...		142	150 ( $\frac{1}{10}$ )
	3.25 p.m.	...		144	150 ( $\frac{1}{10}$ )
	6.25 p.m.	...		142	150 ( $\frac{1}{10}$ )
November 7	12.35 p.m.*	...		150	170 ( $\frac{1}{10}$ )
	6.30 p.m.	...		146	
November 25	12.30 p.m.†	..		154	170 ( $\frac{1}{10}$ )

\* After vomiting. Heart very irregular.

† Had been much troubled with persistent coughing.

This man died about a month after admission. The kidneys were of the cardiac type, and not "granular." The aorta atheromatous. He was much troubled with attacks of coughing and vomiting, which produced the high irregular readings shown above.

TABLE XXI.—Male. Age 60. Aortic disease. Cardiac dilatation.

				Diastolic.	Mean Systolic.	Max. Systolic.
1907						
February 26	8.30 p.m.	...		85 mm.	120 mm.	154( $\frac{1}{8}$ ) mm.
February 27	1.0 p.m.	...		90	120	160( $\frac{1}{8}$ )
February 28	6.50 p.m.	...		88	120	168( $\frac{1}{8}$ )
March 1	2.40 p.m.	...		88	120	158( $\frac{1}{8}$ )
March 2	6.20 p.m.	...		90	118	158( $\frac{1}{8}$ )
March 3	12.50 p.m.	...		88	120	158( $\frac{1}{8}$ )
March 5	6.20 p.m.	...		88	120	158( $\frac{1}{8}$ )

He died a few days later, after an attack of vomiting. Thirty ounces of urine was the maximum amount passed per diem. As a rule the amount measured eighteen ounces.

Marked changes may be observed in the readings of both systolic and diastolic pressure as the result of administration of certain drugs which are used as cardiac stimulants. The drug which is most commonly used in the medical wards by the house-physicians in cases of sudden cardiac failure, whether due to valvular or myocardial disease, is strychnine. The drug is always given hypodermically, and, excepting *in extremis*, there is found a rise in both diastolic and systolic reading within ten minutes, varying according to the degree of failure and the dose of the drug. Long after the heart has failed, as a result of over-distension, to respond to digitalis, this rise in pressure as a result of strychnine medication is noticed, but the effect is apparently more rapid and lasting if a previous venesection has been performed. The systolic blood-pressure apparently rises before the diastolic, and I am, on this account, inclined to think that the drug has an important action upon the cardiac muscle itself, as well as a central vasoconstrictor action upon the blood-vessels. It is only recently that camphor has been used in Guy's Hospital, subcutaneously, for cardiac stimulation; but, as a result of the doses which I have seen employed, the effect upon blood-pressure is insignificant when compared with strychnine. When there are marked signs of right-sided failure, caffeine produces practically no change in either systolic or diastolic pressure, and in cases of less gravity the effect upon the blood-pressure is invariably less than that of strychnine.

In view of the important and exhaustive research which has been carried on by Dixon with regard to the pharmacological action of the digitalis group, it was with considerable interest that I compared the results obtained from the use of digitalis, strophanthus, and squill. Clinically, there is no doubt that digitalis produces its effects more quickly than either squill or strophanthus, slowing the heart's action and increasing the force of the systole. The effect of the administration of digitalis is shown in a marked rise, first of all of the systolic mean pressure, and, later, a rise in the diastolic pressure, though the rise in the latter pressure is frequently delayed four, six, or even ten days, and until it occurs *no* diuretic effect is noticed. The rise in mean

systolic pressure is frequently found to occur within three hours, and is accompanied by a disappearance of the irregular excitable contractions of the heart, which, as it has been mentioned above, are frequently present in cases of "failing heart," and produce maximum systolic readings. Hypodermic injection produces in many cases a marked effect within an hour, though in some cases it is necessary to relieve the distended right heart by means of a venesection. In simple cases of mitral regurgitation a rise of systolic blood-pressure, equivalent to twenty millimetres of mercury, may be noticed within six hours as the result of a single dose of the tincture of digitalis (20 minims) by the mouth. The patient had, in the meantime, been resting in bed.

Strophanthus, administered in pharmacopœal doses, produces very little rise, if any, in diastolic pressure, and a rise in systolic pressure which is transitory and smaller than that produced by digitalis.

Squill, when administered in the form of the official tincture, produces apparently only a slight rise in blood-pressure—and does not seem to produce any alteration of importance in the cardiac rate. This drug is considered by Dixon to be by far the most potent, in pharmacological action, of the three, when tested bio-chemically.

Nitro-glycerin, when administered either by the mouth or hypodermically, produces a marked fall in both systolic and diastolic blood-pressure, but if it is desired that the effect should remain for any length of time, increasing doses are necessary. In one case with which I came in contact the patient, a man of sixty-nine years, was in the habit of taking thirty or more tabloids of nitro-glycerin (B.P.) a day. He had found that, as a result of this medication, attacks of cardiac pain were warded off. He was suffering from arterio-sclerosis with aortic incompetence, and the attacks were apparently due to over-distension of the left ventricle, that is to say, secondary cardiac angina (Douglas Powell). On admission the blood-pressure was found to correspond to 170 mm. systolic and 120 mm. diastolic. It was thought advisable that the administration of the nitrite should be reduced in amount, and reserved for attacks of cardiac pain.

The arterial blood-pressure was estimated every two hours for the first twelve hours, and during this time only four tabloids had been taken. He was by this time anxious and restless, and complaining that if his craving for the drug were not satisfied he would certainly die. The systolic blood-pressure had by this time risen to 190 mm. In eighteen hours the reading was 198 mm.—he had taken one more tabloid, and had obtained some sleep. In another two hours' time it was 202 mm., and he was very anxious.

Twenty-three hours after admission the systolic blood-pressure was found to be 204 mm., and ten minutes later he died suddenly. At the autopsy acute dilatation of the left heart was found. There was atheromatous disease of the aorta and valves; hypertrophy of left ventricle; the coronary arteries were thickened, but their lumen apparently not obstructed. The heart weighed twenty-four ounces. The kidneys showed early interstitial degeneration. I consider that, as a result of heroic doses of nitro-glycerin, the patient was able to exist with an arterial blood-pressure low enough to avoid acute dilatation, and high enough to permit of the performance of renal excretion in a degenerating organ. (Table XXIV.) In other cases of angina pectoris (primary cardiac angina), as a result of nitrite administration, the blood-pressure has fallen below normal, though this is not invariably the case. (Table XXV.) When attacks of palpitation occur, there seems to be a marked fall in diastolic pressure, and an appearance of maximum irregular systolic readings, with slight rise in the systolic pressure sometimes. As a result of the administration of bromides, the irregular "kicking" disappears, and there is a slow rise in diastolic pressure with a steadying of the heart's action. Iodide of potassium possesses apparently the same action in a less degree, and this may account for the disappearance of the throbbing headache of aortic regurgitation which results from the exhibition of that drug.

As a result of the administration of morphia in cases of delirium complicating aortic disease, the slowing of the pulse is accompanied by a rise in diastolic blood-pressure and a

disappearance of irregular systolic readings. Such an effect is only what would be expected from our knowledge of the use of morphia in heart trouble, and I have found similar improvement after the use of hyoscine hydrobromide for aortic delirium. (Table XXVI.)

TABLE XXII.—The effect of strychnine injections upon blood-pressure in a case of acute dilatation. The bag was kept on the arm and the reading taken every two minutes. (Inject. strych. hyp.  $\text{m}\text{viii}\text{j}$ .)

	Diastolic.	Systolic.	Max. Systolic.
1 Before injection ...	?	80	
2 Two minutes afterwards ...	?	80	
3 Four " " ...	?	88	140 once
4 Six " " ...	? 76	90	only
5 Eight " " ...	?	94	
6 Ten " " ...	76	100	152 ( $\frac{1}{2}$ )
7 Twelve " " ...	78	110	
8 Fifteen " " ...	80	120	148 ( $\frac{1}{2}$ )
9 Twenty " " ...	88	128	146 ( $\frac{1}{10}$ )
10 One hour " " ...	90	120	
11 Next day ...	94	126	

I have taken about twenty readings, which show somewhat similar results. This case was one in which the patient seemed absolutely *in extremis*. It was impossible to estimate diastolic pressure. I was of the opinion she was dying. Did strychnine save her life?

Female. Age 32. Aortic disease. Mitral regurgitation.

TABLE XXIII.—The effect of digitalis administered by the mouth. Mitral stenosis and regurgitation. Adult. Aged about 30. Dose: Tinct. digitalis  $\text{3xv}$ . 4 tis. horis. Œdema. Bronchitis. Daily readings.

	Diastolic.	Systolic.	Max. Systolic.	Pulse rate.
1 (On admission) ...	88	118	130 ( $\frac{1}{2}$ )	130
2 " " ...	90	120	—	120
3 " " ...	86	118	140 ( $\frac{1}{10}$ )	122
4 " " ...	88	124	—	116
5 " " ...	88	126	—	112
6 " " ...	94	128	150 once	100
7 " " ...	96*	128	—	104
8 " " ...	100†	128	—	96
9 " " ...	98	130	—	92
10 " " ...	100†	128	—	92
11 Four months later came up to the Surgery	110	134	—	—

\* Presystolic bruit first heard.

† Diuresis began.

‡ Œdema obviously clearing up.

TABLE XXIV.—The effect of nitro-glycerin, in heroic doses, upon the blood-pressure of a man, aged 69, liable to angina pectoris. Dose, self-administration : 30 tabloids B.P. per diem.

			Diastolic.	Systolic.
1	On admission.	12.30 p.m. ...	120	170
2		2.15 p.m. ...	134	174
3		4.0 p.m. ...	134	182
4		6.0 p.m. ...	140	182
5		8.0 p.m. ...	146	184
6		10.0 p.m. ...	142	182
7		Midnight ...	150	190
8		6.0 a.m. ...	160	198
9		8.0 a.m. ...	160?	202
10		10.0 a.m. ...	?	204
11		11.30 a.m. ...	He died.	204 ten minutes before death

Up to midnight (7) only four tabloids had been taken. Up to 6 a.m. (8) one more tabloid allowed.

TABLE XXV.—Female. Age 32. Aortic regurgitation. Angina pectoris. Amyl nitrite inhalations.

			Diastolic.	Systolic.	Max. Systolic.
1	Usual reading	... ...	92	120	
2	After an attack of angina	... ...	82	130	150 ( $\frac{1}{10}$ )
	Amyl nitrite administered.				
3	Another attack	... ...	90	140	146 ( $\frac{1}{8}$ )
	Same treatment.				
4	Another attack	... ...	84	138	
	Same treatment.				
5	Another attack	... ...	78	136	148 ( $\frac{1}{8}$ )
	Same treatment				

The above readings were taken about half an hour after each anginal attack. For obvious reasons it has not been possible to obtain a record during the attack.

TABLE XXVI.—Male. Age 52. Atheroma. Aortic regurgitation and stenosis. Delirium. Readings to show the effect of morphia and hyoscine administration.

	Diastolic.	Systolic.	Max. Systolic.	Pulse per min.	Heart beats per min.
1 Usual reading ...	86	154	170 ( $\frac{1}{10}$ )	90	94
2 Cardiac delirium appeared	82	164	184 ( $\frac{1}{10}$ )	116	128
3 Half an hour after an in- jection of morphia*	90	150	160 ( $\frac{1}{12}$ )	97	98
4 A week later ...	86	148	—	80	82
5 Delirium ...	82	166	180 ( $\frac{1}{10}$ )	120	124
6 Half an hour after an in- jection of hyoscine †	90	130	—	98	98

\* Morphia injection, gr.  $\frac{1}{4}$  + gr.  $\frac{1}{8}$ .

† Hyoscine, gr.  $\frac{1}{200}$ .

The patient died about three weeks later with symptoms of acute dilatation of the heart.



## RENAL DISEASE.

As is well known, one of the first vital reactions to renal insufficiency, whether the latter be due to acute inflammation or chronic degeneration of the kidney, is a rise in arterial blood-pressure. The points investigated were, the extent of such rise in pressure, the duration of the same, the influence of certain complications, and the influence of certain well-recognised forms of treatment upon the readings obtained. Over seventy such cases have been investigated.

All the patients suffering from acute nephritis exhibited signs of general œdema upon admission to the hospital, and, as far as I can tell from the subsequent progress of the cases, and from investigations made upon apparently healthy individuals, the rise in blood-pressure had appeared prior to admission, and had not fallen to a minimal reading until some time after discharge in apparently satisfactory health. Whether this minimal reading was the normal arterial pressure which the patient showed prior to admission, it is impossible to say, but, in certain of the cases which had apparently made a good recovery, I am inclined to think that it remained permanently above normal (Table XXVII.). This rise in arterial blood-pressure, which is an early symptom of acute nephritis, was found in the case of both diastolic and systolic pressures. As will be seen from some of the figures recorded, the actual reading varied a good deal; the average pressures were 130 mm. to 150 mm. diastolic, and 150 mm. to 170 mm. systolic. In some of the cases, however, in which, during the first week, symptoms of cardiac dilatation supervened, there was a sudden fall in pressure, as would be expected, and a more gradual fall in cases of pericardial effusion and œdema of the lungs. I saw one case, terminating with œdema of the larynx and laryngeal obstruction, in which the systolic blood-pressure remained high until about one hour before the patient died, when the last reading was obtained (Tables XXVIII., XXIX., XXX.). Two cases were found in which valvular disease of the heart, due probably to old-standing rheumatic valvulitis, complicated the trouble. One of

these cases, which was fatal, showed the maximum systolic readings which, as I have shown above, are characteristic of the failing heart (Table XXXI.).

Patients suffering from chronic tubal and chronic interstitial nephritis are admitted into the wards at such different stages of disease that readings obtained from them varied a good deal, especially as, in many cases, admission had been obtained on account of the various complications which serve to bring about a fatal termination. As is well known, in both conditions the blood-pressure is higher than normal, but in the case of chronic interstitial nephritis both systolic and diastolic pressures are raised enormously, and it is very characteristic that this high level of arterial pressure is maintained almost up to the onset of uræmic symptoms unless the heart has jibbed previously against the increasing strain.

The patient suffering from chronic interstitial nephritis requires an excessively high blood-pressure, in order that renal functions may be effectively carried out in a damaged organ, and so long as the blood-pressure can be maintained sufficiently high for this purpose, and yet not too high to overtax the muscular reserve power of the heart, he will live in comfort. Unfortunately, very often, as a result of over-exertion, too great a strain is thrown on the left ventricle, the blood-pressure falls, and uræmic symptoms appear (Tables XXXII. and XXXIII.). It is in maintaining a mid-way position between these two extremes that nitro-glycerin is useful, but it will be found that the power of the drug to lower arterial blood-pressure in chronic Bright's disease passes off very rapidly, so that increasing doses are necessary, until, perhaps, thirty-six or forty minims per day are taken (Table XXXV.). I have yet to see, on the autopsy table, a pair of granular kidneys which made any pretence during life to carry out renal functions adequately with a mean systolic blood-pressure lower than 179 mm. More usually the pressure measures 200 mm., and in a considerable number of cases a mean systolic reading of 220 mm. has been obtained with a small wiry, very incompressible pulse, the diastolic blood-pressure measuring not less than 160 mm. As a result of

the use of vapour or radiant heat baths, the blood-pressure apparently falls, considerably in some cases, but it soon afterwards rises again, sometimes to a higher level than before (Table XXXVI.). Injections of pilocarpine produce immediately a fall in blood-pressure with a subsequent rise, varying in amount (Table XXXVII.). But I have not examined a sufficient number of cases to express a definite opinion upon the effect of this drug upon arterial blood-pressure. As a result of the judicious injection of morphia in threatening cases of uræmia, blood-pressure falls with apparent benefit to the patient (Table XXXVIII. and XXXIX.). In some uræmic cases without obvious signs of heart failure, and characterised by drowsiness or coma, with or without convulsions, I have noticed the blood-pressure to remain high until within a few minutes of death (Table XL.). As a result of venesection there was a considerable fall in diastolic and systolic pressure as an immediate result, with a slow return to a slightly lower level than the original reading (Table XLI.).

Albuminuria with pregnancy also claimed attention. When the trouble was due to chronic nephritis, the systolic pressure varied between 180 mm. and 220 mm., and the reading so obtained did not fall appreciably after labour (Table XLII.). In two cases of eclampsia, which recovered after induction of labour, the blood-pressure in each case began to fall immediately after the fœtus had been removed, and slowly returned, in the course of three weeks, to a level which had remained constant on discharge from hospital. One of the patients was seen three months after labour, and there had been no appreciable change in the blood-pressure (Table XLIII.).

TABLE XXVII.—Male. Age 23. Acute nephritis. No complications. Figures refer to pressure measured in millimetres of mercury. Daily estimations. Morning and evening.

				Diastolic.	Systolic.
1	On admission—				
	Evening	...	...	124	156
2	Morning	...	...	130	160
	Evening	...	...	132	158
3	Morning	...	...	132	164
	Evening	...	...	136	166
4	Evening	...	...	132	162
5	Evening*	...	...	130	160
6	Morning	...	...	132	160
7	Evening	...	...	126	158
8	Evening	...	...	120	156
9	Evening	...	...	122	156
10	Evening	...	...	122	156
11	Three days later.	Morning	...	120	154
12	Three days later	...	...	118	148
13	A week later	...	...	118	144
14	A week later	...	...	116	144

\* Albuminuria diminishing. Œdema clearing up. Subsequent recovery.

TABLE XXVIII.—Male. Age 21. Acute tubal nephritis. Cardiac dilatation.

				Diastolic.	Systolic.
1	(On admission)	...	...	140	170
2	...	...	...	138	164
3	...	...	...	138	166
4	...	...	...	138	166
5*	...	...	...	140	168
6	...	...	...	134	164
7	...	...	...	126	150
8†	...	...	...	124	148
9	...	...	...	122	148
10	...	...	...	130	156
11	...	...	...	124	148
12	...	...	...	120	144
13	...	...	...	126	150
14	...	...	...	130	154

\* Patient distressed. Œdema increasing. Drowsy. Heart's action more rapid.

† Physical signs of cardiac dilatation.

The readings were taken daily. Subsequently the patient made slow progress. The œdema cleared up, and he was discharged with a trace of albumin in the urine.

**TABLE XXIX.**—Female. Age 33. Tubal nephritis. Daily readings, morning and evening.

			Diastolic.	Systolic.
1	On admission	... ..	134	170
2	Morning	... ..	134	170
	Evening	... ..	132	172
3	Morning	... ..	134	174
	Evening	... ..	134	176
4	Morning	... ..	130	174
	Evening	... ..	126	170
5	Morning	... ..	122	160
	Evening	... ..	122	162
6	Evening	... ..	120	160
7	Evening	... ..	120	156
8	Morning*	... ..	120	154
9	Evening	... ..	122	156
10	Morning†	... ..	122	154
	Evening	... ..	120	154

\* Signs of pericarditis.

† Obvious signs of pericardial effusion.

She subsequently went from bad to worse, general anasarca developed, and death occurred seventeen days after admission.

**TABLE XXX.**—Male. Age 22. Acute nephritis. Uræmia. Œdema of larynx. Anasarca.

			Diastolic.	Systolic.
1	On admission, mid-day	... ..	142	172
	10.0 a.m.	... ..	140	174
2	8.0 a.m.	... ..	142	176
	10.0 a.m.	... ..	144	178
	12.30 p.m.	... ..	142	178
	6.0 p.m.	... ..	146	180
	8.0 p.m.	... ..	146	176

Died at 9.30 p.m.

**TABLE XXXI.**—Male. Age 15. Acute nephritis. Mitral regurgitation.

			Diastolic.	Systolic.	Max. Systolic
1	Admission	... ..	122	152	150 ( $\frac{1}{8}$ )*
2	...	... ..	126	148	
3	...	... ..	120	146	158 ( $\frac{1}{8}$ )
4	...	... ..	118	132	162 ( $\frac{1}{8}$ )
5	...	... ..	116	132	160 ( $\frac{1}{8}$ )

\* Indicates one beat in six.

Daily readings. He died about fourteen days later.

TABLE XXXII.—Male. Age 58. Granular kidney. Daily readings.

					Diastolic.	Systolic.
1	On arrival	...	...	...	168	200
2	...	...	...	...	164	200
3	...	...	...	...	166	194
4	...	...	...	...	168	198
5	...	...	...	...	170	204
6	...	...	...	...	174	210
7	...	...	...	...	180	220
8	...	...	...	...	174	216
9	...	...	...	...	178	218
10*	...	...	...	...	180	220
11	...	...	...	...	178	208
12†	...	...	...	...	180	216
13	...	...	...	...	178	210

\* Patient becoming drowsy.

† Practically unconscious.

He died a few hours after the last reading was taken. An example of blood-pressure remaining high. With uræmic symptoms.

TABLE XXXIII.—Male. Age 64. Granular kidney. Fibroid heart, cardiac dilatation. Uræmia. Daily readings.

					Diastolic.	Systolic.	Max. Systolic.
1	...	...	...	...	170	206	178 ( $\frac{1}{2}$ )
2	...	...	...	...	172	200	
3	...	...	...	...	174	208	
4	...	...	...	...	174	210	
5	...	...	...	...	172	216	
6	...	...	...	...	164	198	
7	Morning	...	...	...	162	194	
	Evening	...	...	...	160	194	
8	Morning	...	...	...	152	180	
	Evening	...	...	...	148	176	
9	Evening	...	...	...	136	164	
10	Morning	...	...	...	140	162	
11	Evening	...	...	...	134	158	
12	Evening	...	...	...	132	158	
13	Evening	...	...	...	118	144	

An example of falling arterial blood-pressure, due to cardiac dilatation, resulting in renal insufficiency and uræmia. He died of uræmia two days after the last reading.

TABLE XXXIV.—Male. Age 58. Mitral regurgitation. Chronic interstitial nephritis. Cardiac dilatation.

			Diastolic.	Mean Systolic.	Max. Systolic.
1	6.30 p.m.	...	120	138	160 ( $\frac{1}{2}$ )
2	5.20 p.m.	...	122	150	
3	5.35 p.m.	...	120	152	
4	6.30 p.m.	...	120	150	
5	6.35 p.m.	...	124	154	
6	12.50 p.m.	...	122	150	

Taken in six successive days. A month afterwards, upon discharge, there was practically no change, and almost the same readings were obtained on his admission under Dr. Pitt three months later.

TABLE XXXV. Male. Age 65. Chronic interstitial nephritis. Cerebral hæmorrhage, resulting in paralysis of left arm and left side of face. Nitro-glycerin employed in increasing doses to relieve headache and lower blood-pressure. Daily readings:—

	Diastolic.	Systolic.	Max. Systolic.	Dose of Drug.
1 On admission...	160	178	180( $\frac{1}{2}$ ) 194( $\frac{1}{8}$ )	Liq. Trinitrini mii. tds
2 ...	150	168	180( $\frac{1}{2}$ )	
3 ...	150	172	180( $\frac{1}{2}$ )	
4 ...	156	176	190( $\frac{1}{2}$ )	L. T. mii. 6tis.
5 ...	154	178	190( $\frac{1}{2}$ )	horis.
6 Two days later	162	180	200( $\frac{1}{2}$ )	
7 Next day	164	188	200( $\frac{1}{2}$ )	
8 Two days later	174	196	218( $\frac{1}{2}$ )	L. T. mii. 4tis.
9 Next day	174	196	216( $\frac{1}{2}$ )	horis.
10 Next day	176	198	216( $\frac{1}{2}$ )	L. T. miiij. 4tis.
11 Two days later	154	180	—	horis.
12 Next day	154	176	180( $\frac{1}{2}$ )	
13 Two days later	165	184	190( $\frac{1}{2}$ )	
14 Next day	170	196	210( $\frac{1}{2}$ )	L. T. miv. 4tis.
15 Three days later	152	174	—	horis.
16 Next day	154	176	—	
17 Three days later	160	188	194( $\frac{1}{2}$ )	
18 Two days later	172	196	208( $\frac{1}{2}$ )	L. T. mvi. 4tis.
19 Next day	140	150	165( $\frac{1}{8}$ )	horis.
20 Next day	140	150	160	
21 Two days later	160	178	190( $\frac{1}{2}$ )	
22 Next day	160	178	190( $\frac{1}{2}$ )	
23 Two days later	162	178	190	

He was discharged relieved. Subsequently readmitted, and again relieved. Increasing doses of the nitrite were necessary to relieve headache and lower blood-pressure. His normal blood-pressure is probably considerably higher than is here represented.

He was readmitted yet a second time in June, 1908, that is to say, a year after his first admission. And at the present time (July 15th, 1908), he is suffering a great deal from dyspnœa, with obvious signs of cardiac failure, œdema of the legs, etc. There is a marked difference in the height of the arterial blood-pressure. Digitalis has been administered, but there has been no tendency towards improvement.

The following readings have been taken :—

					Diastolic.	Mean Systolic.	Max. Systolic.
1908							
1	June 16	...	...	...	100 mm.	124 mm.	136 mm. ( $\frac{3}{4}$ )
2	June 22	...	...	...	100 mm.	122 mm.	140 mm. ( $\frac{1}{2}$ )
3	July 15	...	...	...	98 mm.	126 mm.	136 mm. ( $\frac{1}{2}$ )

July 15th. At the present time he is thought to be dying.

NOTE.—November, 1908. The man died on July 21st last, with signs of cardiac failure. There was marked arterio-sclerosis, especially of the cerebral vessels, and evidence of an old hæmorrhage in the left side of the brain. The heart, which was hypertrophied and dilated with fibrotic change, weighed 630 grms. No evidence of valvular disease. The kidneys weighed 356 grms.; vessels sclerosed. Fibrotic and cystic change in the cortices, with granular surfaces. (Inspection, 1908, 374.)

TABLE XXXVI.—Boy. Age 16. Chronic tubal nephritis. Anasarca. Albuminuria. Casts, etc. Readings to show effect of a radiant heat bath upon blood-pressure, taken every five minutes.

					Diastolic.	Systolic.
1	Usual reading	...	...	...	146	172
2	Start	...	...	...	144	172
3	Lights on	...	...	...	144	170
4	Five minutes	...	...	...	144	172
5	Ten minutes	...	...	...	144	172
6	Fifteen minutes	...	...	...	136	168
7	Twenty minutes	...	...	...	132	164
8	Twenty-five minutes	...	...	...	126	160
9	Thirty minutes*	...	...	...	128	160
10	Forty-five minutes	...	...	...	130	164
11	Sixty minutes	...	...	...	130	164
12	Ninety minutes	...	...	...	140	168
13	Two hours	...	...	...	144	168
14	Four hours later	...	...	...	146	176

\* Lights out.



**TABLE XXXVII.**—To show effect of pilocarpine injections.  
**Male. Age 53. Arterio-sclerosis. Hypodermic injection, gr.  $\frac{1}{2}$ . Pilocarpine nitrate.**

14th November, 1906.

6.25 a.m.	Mean systolic pressure	...	...	142 mm.
6.15 p.m.	Five minutes after injection	...	...	118
6.20 p.m.	Sweating	...	...	130
6.25 p.m.	...	...	...	150

15th November, 1906.

6.15 p.m.	Injection.	Mean systolic	...	140
6.20 p.m.	...	...	...	130
6.22 p.m.	...	...	...	125
				(Began to sweat.)
6.25 p.m.	...	...	...	148
6.30 p.m.	...	...	...	170

16th November, 1906.

6.50 p.m.	Mean systolic at	...	...	138
6.55 p.m.	Injection 6.53 p.m.	...	...	128
7.0 p.m.	...	...	...	125
7.5 p.m.	Began to sweat slightly	...	...	138
7.10 p.m.	...	...	...	138
7.15 p.m.	...	...	...	138
8.30 p.m.	...	...	...	125

Injection had very little effect.

19th November, 1906.

6.20 p.m.	Mean systolic	...	...	146
6.30 p.m.	...	...	...	140
6.35 p.m.	...	...	...	140
6.45 p.m.	...	...	...	146

Injection at 6.15 p.m. No effect.

20th November, 1906.

Injection doubled. Pilocarpine nitrate gr.  $\frac{1}{2}$ , at 6.20 p.m.

6.15 p.m.	...	...	...	140
6.25 p.m.	...	...	...	138
6.30 p.m.	...	...	...	136
6.35 p.m.	Sweating well	...	...	140
6.40 p.m.	...	...	...	150
6.45 p.m.	...	...	...	155

TABLE XXXVIII.—Injection of morphia. Female. Age about 30. Pregnancy 8 months. Uræmic symptoms. Eclampsia. Daily readings:—

			Diastolic.	Systolic.
1	On admission	... ..	155	190
	Same evening	... ..	154	186
2	Morning, * 10 a.m.	... ..	142	172
	Evening, 6 p.m.	... ..	140	172
3	Morning, † 10.15 a.m.	... ..	138	168
	Evening, 6.30 p.m.	... ..	138	166
4	Morning	... ..	142	170
5	Evening	... ..	144	170
6	Evening†	... ..	156	194
7	Evening	... ..	154	192

\* I.M.H. gr.  $\frac{1}{2}$ , given about 5 a.m.

† Two further injections of morphia, to check convulsions (about 6 a.m.).

‡ Signs of pulmonary engorgement.

She died next morning.

TABLE XXXIX.—Male. Age 46. Chronic interstitial nephritis. Uræmic delirium. Daily readings. Morphia.

			Diastolic.	Systolic.
1	Usual reading	... ..	180	218
2	Vomiting, headache, drowsiness	... ..	178	222
3	Much the same	... ..	178	220
4	Delirious, afternoon*	... ..	180	224
	Evening, 6.30	... ..	168	190
5	Morning	... ..	166	188
	Evening	... ..	164	188
6	Evening	... ..	170	192

\* I.H.M. gr.  $\frac{1}{2}$  +  $\frac{1}{8}$ , given about 4.30 p.m.

He died about three weeks later. Granular kidneys; small. Hypertrophied heart.

TABLE XL.—Male. Age 46. Chronic interstitial nephritis. Uræmia. Daily readings for five days before death. Treatment by purging ; radiant heat baths.

				Diastolic.	Systolic.
1	Usual reading	...	...	170	200
2	Morning	...	...	168	198
	Evening	...	...	172	202
3	Morning*	...	...	172	208
	Evening	...	...	172	210
4	Morning†	...	...	170	212
	Evening	...	...	172	216
5	Morning‡	...	...	176	222
	Evening	...	...	176	218
6	Morning	...	...	178	222

\* Increasing headache, drowsiness, sickness.

† Has had one or two slight convulsions—can only be roused with difficulty.

‡ Unconscious. Cheyne-Stokes' breathing. Note that the arterial blood-pressure remained high until within half an hour of death.

He died half an hour later.

TABLE XLI.—Venesection. Case, "granular kidney." Male. Age 45. Headache. Vomiting. Daily estimations:—

				Diastolic.	Systolic.
1	Usual reading	...	...	168	196
2	Morning	...	...	174	202
	Evening	...	...	178	206
3	Morning	...	...	176	200
	Evening	...	...	176	200
4	Morning, 10.0 a.m.	...	...	178	200
	12.30 p.m.	...	...	178	200
	Venesection 2.15 p.m., one pint.				
	2.30 p.m.	...	...	148	176
	5.30 p.m.	...	...	150	176
	8.30 p.m.	...	...	160	186
	11.30 p.m.	...	...	158	188
5	8.30 a.m.	...	...	158	186
	12.30 p.m.	...	...	158	180
6	12.30 p.m.	...	...	158	182

TABLE XLII.—Pregnancy, with chronic tubal nephritis. Female. Age 32. Parturition at eight and a half months.

			Diastolic.	Systolic.
1	On admission	... ..	148	180
2	Second day	... ..	150	186
3	Third day	... ..	152	184
	Parturition.			
	Evening reading	... ..	148	184
4	Fourth day	... ..	146	178
5	Fifth day	... ..	148	176
6	Sixth day	... ..	144	176
7	Tenth day	... ..	146	178
8	Fifteenth day	... ..	146	180
9	Three weeks later	... ..	146	176
10	One month	... ..	148	174

Blood-pressure remains high. Patient subsequently transferred to medical wards. Albuminuria. Casts. Relapsing œdema. Convalescence.

TABLE XLIII.—Female. Age 35. Admitted for eclampsia. Morphia administered. Induction of labour.

			Diastolic.	Systolic.
1	On admission	... ..	138	178
	Evening	... ..	136	180
	Delivery.			
2	Morning	... ..	140	180
	Evening	... ..	144	180
3	Morning	... ..	130	160
	Evening	... ..	128	162
4	Morning	... ..	132	164
	Evening	... ..	130	166
5	Morning	... ..	132	158
	Evening	... ..	132	160
6	Morning	... ..	124	150
	Evening	... ..	124	152
7	Morning	... ..	118	146
	Evening	... ..	118	144
8	A week later	... ..	116	140
9	A week later	... ..	100	136

Subsequently did very well. Shows the steady fall in blood-pressure as patient recovers. Compare with Table XLII. Chronic tubal.

## ADDISON'S DISEASE.

There have been three cases of this disease in Guy's Hospital during the past two years, in which the diagnosis has been verified at the autopsy. In all these cases arterial blood-pressure was certainly very low, though in one of the three, which died shortly after admission, the actual value was not obtained. In the case here recorded (Table XLIV.) the patient's symptoms were absolutely typical; he was nearly always to be found curled up, asleep, under the bedclothes. When he was awake, it appeared to be too much trouble for him to speak or to feed himself. Occasionally he would answer questions in a drowsy, dreamy way. His maximum systolic blood-pressure never measured more than eighty millimetres of mercury at any time during the month in which we were examining him. The mean systolic pressure at times was as low as forty-eight millimetres. It was quite impossible to estimate the diastolic pressure. The patient was a young fellow of twenty, well grown, strong and healthy prior to the onset of his fatal illness.

TABLE XLIV.—Male. Age 20. Addison's disease. This is the lowest series of blood-pressure readings which we have obtained. It was quite impossible to estimate diastolic pressure.

			Mean Systolic.	Max. Systolic,
1907				
November 12	6.0 p.m.	...	65 mm.	70 mm. (†)*
	9.45 p.m.	...	60	65
November 13	5.30 p.m.	...	60	70 (‡)
November 14	12 noon	...	60	70 (‡)
November 15	1.0 p.m.	...	60	70 (‡)
	6.30 p.m.	...	58	68
November 18	12.50 p.m.	...	70	80
	5.50 p.m.	...	68	76
November 19	5.15 p.m.	...	65	72
	9.45 p.m.	...	62	70
November 20	1.0 p.m.	...	48	—
November 21	6.30 p.m.	...	58	70
November 22	3.0 p.m.	...	60	70

\* Indicates one beat in five.

He died a few days later. Figures indicate pressure in millimetres of mercury.

EXOPHTHALMIC GOITRE.

Twelve cases were examined; eight of them were women. In all of them the diastolic pressure was apparently lower than normal; there were occasional irregular maximum readings. The systolic mean pressure was high, but it was only sustained for a very small part of the cardiac circle, so that the readings obtained were similar to those noted in aortic disease.

TABLE XLV.—Female. Age 26. Symptoms of Graves' disease had been present for two years. Daily readings.

	Diastolic.	Systolic.	Max. Systolic.
1 ... ..	84	150	174 ( $\frac{1}{2}$ )
2 ... ..	86	148	
3 ... ..	82	152	
4 ... ..	80	152	
5 ... ..	84	152	
6 ... ..	84	152	
7 ... ..	84	150	
8 ... ..	86	152	
9 ... ..	88	154	
10 ... ..	84	154	
11 ... ..	84	154	
12 ... ..	86	156	
13 ... ..	84	160	
14 ... ..	82	156	
15 ... ..	84	154	
16 ... ..	84	156	
17 ... ..	84	156	
18 ... ..	82	156	
19 ... ..	82	154	
20 ... ..	84	154	

TABLE XLVI.—Female. Age 26. Symptoms of Graves' disease had been present for three years. Daily readings. Treatment. Rest in bed. Belladonna.

	Diastolic.	Systolic.	Max. Systolic.
1 Evening ... ..	88	142	164 ( $\frac{1}{2}$ )
2 Evening ... ..	90	146	—
3 Evening ... ..	94	148	—
4 Morning ... ..	88	148	—
5 Evening ... ..	92	140	164 ( $\frac{1}{2}$ )
6 Evening ... ..	90	148	160 ( $\frac{1}{2}$ )
7 Evening ... ..	90	148	—
8 Evening ... ..	90	146	—
9 Three weeks later	96	136	—
Evening ... ..	96	138	—
10 Evening ... ..	94	136	—
11 Evening ... ..	96	136	—
12 Evening ... ..	96	136	—

## LOBAR PNEUMONIA.

A few observations were made upon cases of lobar pneumonia. Certainly, in one of the cases examined, the arterial blood-pressure remained high until within about half an hour of death. The patient was unconscious, and suffering apparently from general pneumococcal poisoning. (Table XLVII.) One case of pneumonia complicated by mitral disease is here given. The subject was a young male adult, and the blood-pressure readings merely seem to confirm the opinions given elsewhere as to the changes which may be expected with a failing heart. (Table XLVIII.) In other cases in which there was obvious right-sided cardiac dilatation with pulmonary congestion, though the systolic mean pressure was high (160 mm., 165 mm., 170 mm. were recorded), such pressure was only maintained for a very small part of the systolic period of the cardiac cycle, and was therefore, we may suppose, of little benefit to the patient. (Table XLIX.) Strychnine, when administered hypodermically, invariably produced a rise in arterial pressure with steadying of the heart's action. From what I have seen of adrenalin, as used in the wards, the effect produced is variable, and quickly passed off, so that the same improvement in the pulse was not noticed. With caffein, the effect was variable also, but when a rise in blood-pressure was obtained it was more usually sustained than was the case with adrenalin. A good many cases, of course, were in such a serious condition that I was unable to obtain any consecutive estimations at regular intervals.

TABLE XLVII.—Male. Age 28. Double pneumonia. Pneumococcal septicæmia. Death.

					Diastolic.	Systolic.	Max. Systolic.
1	5.30 p.m.	...	...	...	116	144	—
	9.30 p.m.	...	...	...	120	150	170 ( $\frac{1}{10}$ )
2	8.30 a.m.	...	...	...	118	146	170 ( $\frac{1}{10}$ )
	10.0 a.m.	...	...	...	122	148	—
	12.0 noon	...	...	...	120	148	—
	4.0 p.m.	...	...	...	120	150	—

Died half an hour later.

TABLE XLVIII.—Male. Age 28. Lobar pneumonia. Mitral regurgitation. Daily readings.

				Diastolic.	Systolic.	Max. Systolic.
1	Evening	...	...	92	126	150 ( $\frac{1}{2}$ )
2	Morning	...	...	90	130	148 ( $\frac{1}{2}$ )
3	Evening	...	...	90	124	148 ( $\frac{1}{10}$ )
4	Evening	...	...	88	124	148 ( $\frac{1}{2}$ )
5	Morning	...	...	90	124	148 ( $\frac{1}{2}$ )
	Evening	...	...	90	126	146 ( $\frac{1}{10}$ )
6	Morning	...	...	90	126	146 ( $\frac{1}{2}$ )
	Evening	...	...	90	126	148 ( $\frac{1}{2}$ )
7	Evening	...	...	94	124	146 ( $\frac{1}{10}$ )
8	Evening	...	...	98	126	150 ( $\frac{1}{2}$ )
9	Evening	...	...	98	128	144 ( $\frac{1}{2}$ )

Subsequently did well.

TABLE XLIX.—Male. Age 38. Alcoholic. Double pneumonia. Right-sided cardiac dilatation. No valvular disease.

				Diastolic.	Systolic.
1	Evening	...	...	102	162
2	Morning	...	...	98	160
	Evening	...	...	96	160
3	Morning	...	...	100	160
	Evening	...	...	96	164
4	Morning	...	...	94	160

He died later in the day. The systolic reading is high, but it is not sustained for more than a short part of the systolic period. Compare readings with those from cases of aortic regurgitation.

TABLE L.—Female. Age 32. Lobar pneumonia. Strychnine injections.

				Diastolic.	Systolic.
1	Mid-day	...	...	102	124
	5.30 p.m.	...	...	94	118
	8.30 p.m.	...	...	110	134
	11.30 p.m.	...	...	110	140
2	10.15 a.m.	...	...	112	140
	12.30 p.m.	...	...	110	138
3	4.30 p.m.	...	...	110	138
4	6.0 p.m.	...	...	110	140

At 6.0 p.m. on the first day (fourth of the disease), owing to increasing cyanosis, strychnine injections were ordered. I.S.H. m. v. 3tis horis. Subsequently did well.



## PREGNANCY.

The final series of observations which I have to record are in association with a physiological state, and not with a disease. I have already mentioned certain alterations which may be noticed in connection with chronic tubal nephritis, and the toxic nephritis of pregnancy. It was obviously necessary to find out if there was any tendency for alterations in arterial pressure to occur in cases of normal labour. Two dozen consecutive cases of pregnancy in Queen Victoria Ward were examined. In some of them no difficulties were anticipated or experienced during parturition; in others, though trouble had been anticipated, none was experienced. In all of these cases a slow rise in both systolic and diastolic pressure was found, which reached a maximum with the onset of the first stage of labour. After labour blood-pressure is apparently subnormal for a time, and then there is a slow rise to normal level during the early stages of the puerperium. While labour is in progress the blood-pressure between the pains is apparently low, but there was considerable difficulty in estimating its value while uterine contractions were taking place, owing to muscular movements in the extremities. Apparently it rises considerably. In one case of mitral stenosis with pregnancy, very low readings were obtained, and some œdema of the feet, with bronchitis, developed, but the patient subsequently rallied and did quite well. Ergot, when administered for gynaecological purposes, either subcutaneously or by the mouth, does not appear to produce a general arterial rise in blood-pressure. (Tables LI., LII.)

TABLE LI.—Pregnancy. Labour. Patient aged 26. 2 para. Morning and evening readings. Labour normal.

				Diastolic.	Systolic.
1	Evening	...	...	98	126
2	Morning	...	...	98	126
	Evening	...	...	100	126
3	Morning	...	...	98	130
	Evening	...	...	108	130
4	Morning	...	...	110	136
	Evening	...	...	116	140
5	Morning	...	...	114	144
	Evening	6.30 p.m.	...	120	150
		8.30 p.m.	...	118	150
		11.0 p.m.*	...	122	150
6	Evening	...	...	100	126
7	Two days later	...	...	94	126
8	Two days later	...	...	94	124

\* First stage of labour. 9.30 p.m. Child born at 4 a.m. next day.

TABLE LII.—Patient aged 28. 3 para. Pregnancy and labour normal.

				Diastolic.	Systolic.
1	Morning	...	...	94	120
	Evening	...	...	96	120
2	Morning	...	...	96	120
	Evening	...	...	96	122
3	Morning	...	...	100	128
	Evening	...	...	100	128
4	Morning	...	...	110	134
	Evening	...	...	112	134
5	Morning	...	...	110	136
	Evening*	...	...	110	138
6	Evening	...	...	90	120
7	Morning	...	...	92	120
	Evening	...	...	90	120

\* Labour. First stage. Child born six hours later.

## CONCLUSIONS.

1. Arterial blood-pressure, both systolic and diastolic, varies much in different individuals, at different ages, with rest and exercise, in health and disease, at different hours of the day.

2. The difference between systolic and diastolic readings, in most healthy individuals, measures about thirty millimetres of mercury.

3. In the case of individuals who are "untrained," vigorous muscular exercise is accompanied by a rise in the systolic arterial pressure with high irregular readings, which are maintained during only a small portion of the cardiac systolic period. The diastolic pressure remains low, or rises very slowly. Similar changes, less marked in degree, were found in the case of individuals who had taken exercise immediately after meals. The phenomenon of "second wind" is accompanied by a rise in diastolic arterial pressure, with a disappearance of the high irregular systolic readings above mentioned.

4. When there is valvular disease of the heart and compensation fails, the diastolic blood-pressure falls steadily, and

irregular maximum systolic readings appear. If the valvular disease is of long standing, and has been accompanied by hypertrophy of the left ventricle, the mean systolic pressure may remain normal or above normal for some time, but this level is only maintained for a very small fraction of the systolic period, and there is a rapid fall with the onset of cardiac dilatation or pericardial effusion.

5. Blood-pressure readings taken after a cardiac patient has been allowed to get up for the first time show a rise in the value of the mean systolic pressure, which rise is smaller as improvement in general health is maintained. If a fall in diastolic pressure is registered, it is an indication that the patient has been allowed to get up too soon.

6. The appearance of the presystolic bruit in cases of mitral stenosis is always accompanied by a rise in the mean diastolic pressure, and until the mitral mid-diastolic bruit of the failing heart has given way to the mitral presystolic bruit, such improvement does not take place.

7. In cases of myocardial degeneration, both systolic and diastolic blood-pressures are of low value, and there is not the same tendency to high, short, irregular systolic "kicking."

8. Venesection.—When the quantity of blood removed from the arm, in cases of advanced mitral failure, was eight ounces or under, there was practically no change noticed in either diastolic or systolic pressure. When the quantity of blood removed was ten ounces or over (up to twenty-three ounces) the immediate effect of the venesection was a rise in the mean systolic pressure, a steadying of the heart's action, with a disappearance of irregular maximum systolic readings. After about four hours' time a rise was also noticed in diastolic arterial pressure.

9. Strychnine and digitalis, when administered in cases of heart disease, produced greater effects upon arterial blood-pressure, as cardiac stimulants, than any other drugs which we have seen employed. Nitro-glycerin, in large doses, is very useful for lowering blood-pressure in cases of secondary cardiac angina, but increasing doses are necessary if the effect is to be maintained.

Morphia frequently produces a rise in diastolic blood-pressure, with a steadying of the heart's action, and a similar improvement may be noticed after the use of hyoscine for aortic delirium.

10. With acute nephritis, but more especially with chronic interstitial nephritis, both diastolic and systolic pressures are enormously increased, the former relatively more than the latter. This high reading is maintained in many cases, even after the onset of uræmic symptoms, and may only fall a few minutes before death. If the left ventricle has given way against the constant strain, blood-pressure falls towards normal, and, in any case, a rapid fall in arterial pressure indicates the closing scene.

11. The onset of the first stage of labour is preceded by a rise in both systolic and diastolic pressure.

12. The lowest readings recorded of any of the cases investigated were obtained in a case of Addison's disease.

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The subject-matter of the foregoing article has been obtained as a result of some observations made by myself upon patients in Guy's Hospital during the past two years. For permission to investigate the cases I am much indebted to the physicians and surgeons to the hospital, and especially to Dr. Frederick Taylor, who, while senior physician, and later as consulting physician, has helped me with many kindly criticisms and comments.



# THE BLASTOCYST OF CAPRA.

WITH

SOME REMARKS UPON THE HOMOLOGIES OF THE  
GERMINAL LAYERS OF MAMMALS.

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## THE BLASTOCYST OF CAPRA HIRCUS.

I HAVE a few specimens of goat embryos in the early stages of development which may be worthy of record, although they show that the blastocyst of the goat differs only in a slight degree from that of kindred ungulates such as the sheep or deer.

Since, however, there is no description at all of the blastocyst of Capra, and as I do not see my way to obtain more specimens at present, it seems as well to make what use I can of the stages, four in number, in my possession. These specimens were the result of killing five goats supposed to have been pregnant about five to nine days.

The following table gives the specimens found in each case, and the corpora lutea noticed in the ovaries:—

Age.	Corpora lutea.		Embryos found.
	Right ovary.	Left ovary.	
No. 1. 5 days ...	1	—	—
No. 2. 5 days 20 hours ...	1	1	2
No. 3. 6 days 16½ hours ...	—	1	1
No. 4. 9 days ...	—	1	2
No. 5. A day or two older ...	—	1	1

The specimens were obtained in the same manner as I obtained those of the sheep and pig, namely, by injecting the horns of the uterus with .5 per cent. chromic acid containing a trace of osmic acid within fifteen minutes of the death of the animal. Then, after immersion of the whole uterus thus distended for some days in .5 per cent. chromic acid, I searched with a microscope through the fluid released from the cavity of the uterus.

I will take the youngest stage first.

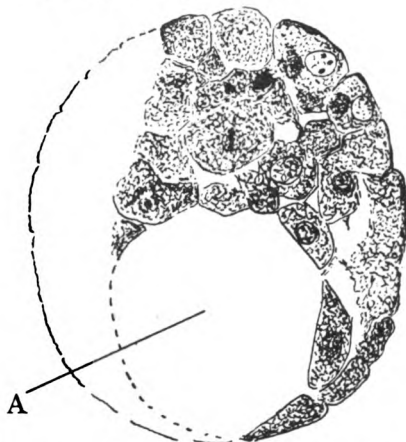


FIG. 1.—Vertical section of the blastocyst of the goat. Age, 5 days, 28 hours. The blastocyst was broken; the missing part is indicated in outline. A, archenteron.  $\times 400$ .

This was specimen No. 2, the age being five days twenty hours. Two corpora lutea were visible, and therefore the expectation was for two embryos. Unfortunately the uterus had been too slightly distended by the fluid injected, which led to the destruction, more or less complete, of the two blastocysts which were found. One was hopelessly injured, the other was broken, but such part as was saved was in excellent histological condition. The blastocyst is in an early stage equivalent to that of the sheep of five and three-quarter days (Assheton,<sup>2</sup> Fig. 15) or pig five days three hours (Assheton,<sup>3</sup> Fig. 17). The dates are to be regarded as approximate only, but they suffice to show that in these three ungulates there is a close parallelism in time with reference to the development of the embryo.

Fig. 1 gives an idea of the condition of the specimen with the missing side indicated in outline. I have no doubt that in this specimen the future ectoderm cells are imbedded among or between the future trophoblast and hypoblast cells, but there is no means of identifying them as yet.

The cells resemble those of the sheep's blastocyst rather than the pig's in being larger, more clearly delimited, and more homogeneous in character. The resemblance to my figure of the sheep's blastocyst (Fig. 15) is very close, except for the zona radiata which, in my broken specimen of the goat, is probably absent by accident only.

The clearly-defined nature of the blastocyst cavity or archenteron, as I prefer to call it, is marked. The definitive inner mass is not, so far, separated from the rest. The inner mass at present constitutes about two-thirds of the wall of the blastocyst, only one-third being as yet monodermic. In other words, out of some

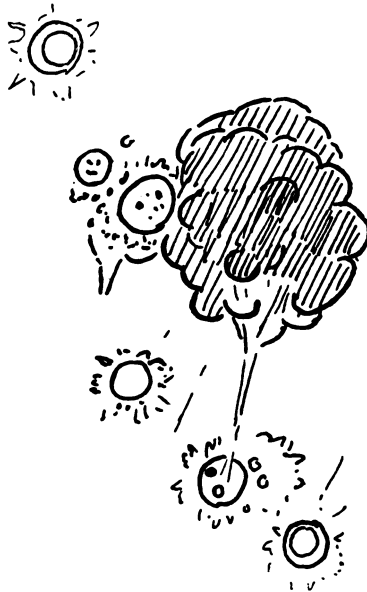


FIG. 2. Inner mass of blastocyst of goat seen from within. Age, 9 days. The inner cell of the inner mass is connected by a strand of protoplasm with a trophoblast cell.



one hundred or more cells forming the blastocyst, about sixty go to form the thickened side. Since in the subsequent stage only some twenty cells form the epiblastic rudiment, it follows that the epiblastic cells, if they are already differentiated from the trophoblast and hypoblast, form only a small proportion of the inner mass, which contains not more than forty cells in the next stage.

Presumably, then, the wall of the blastocyst of this later stage is partly increased at the expense of cells and their descendants now forming a portion of the inner mass. This view is rendered the more probable by such appearances as that shown in Fig. 2, where connecting strands of protoplasm may be seen passing from the inner layer of the inner cell-mass to the wall-cells, suggesting at the same time a community of origin and a drawing out and away of the more lateral cells of the inner mass into the monodermic wall of the blastocyst.

Specimen 3. Age 6 days, 16½ hours.

This specimen corresponds to my Fig. 16 of the sheep and 19 of the pig, and is still earlier than any of Keibel's<sup>14</sup> specimens of the roe deer figured in his paper in the *Archiv. f. Anat. u. Physiologie*. A considerable advance has been made upon the previous specimen. The embryo is a typical blastocyst having a wall of a single layer of attenuated cells with an inner cell-mass attached to one pole. The wall-cells are very much stretched and vary in size and shape, and are 4, 5, 6, or 7-sided. The largest cell is on the lower pole. The form was almost a sphere, the longest and shortest diameters being represented by the figures 20.9 and 21 respectively. The germinal area had a longer and shorter axis measuring proportionately 5 and 4.5. The blastocyst was so smooth and regular in form that probably a zona was present, but much attenuated. I cannot, however, detect it for certain in the sections. The edge of the inner mass was more abrupt at one end than the other. The blastocyst was cut into sections, ten of which show the inner mass. Fig. 3 is a drawing of the fifth.

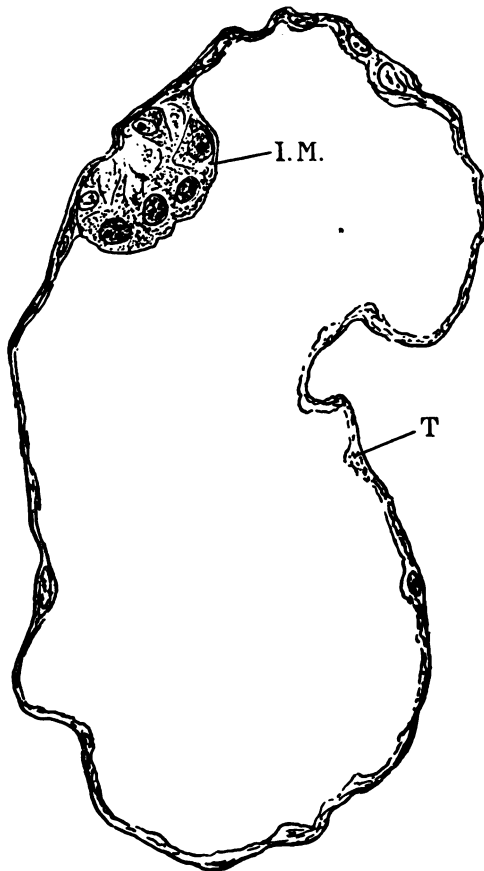


FIG. 3.—Vertical section through a blastocyst of the goat. Age, 6 days, 16½ hours. The inner mass forms a swelling at one point of the otherwise monodermic vesicle. I.M., inner mass; T, trophoblast;  $\times 400$ .

There is no doubt that in every section the trophoblast is to be seen quite distinctly overlying the inner mass. It is not possible to distinguish between epiblast and hypoblast with certainty, though in some sections there are cells which may be regarded with some confidence as hypoblast, and in one or two sections cells which may be described as probably epiblast.

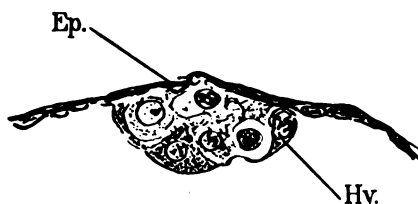


FIG. 4.—Transverse section through the embryonic mass of the goat. Age, 6 days,  $16\frac{1}{2}$  hours. It is the same specimen as in Fig. 3. It shows, perhaps, a differentiation into epiblast and hypoblast. Ep., epiblast; Hy., hypoblast. The line, Ep., should have been continued another  $\frac{1}{8}$  inch.  $\times 400$ .

Specimen 4. Capra 4. Age 9 days. (Embryo No. 2.) Only one ovary, the left, showed a corpus luteum, but two blastocysts were found, and both in the left horn of the uterus. Each horn was separately filled with chromic acid .5 per cent., and a trace of osmic acid, within 10 minutes of the death of the animal.

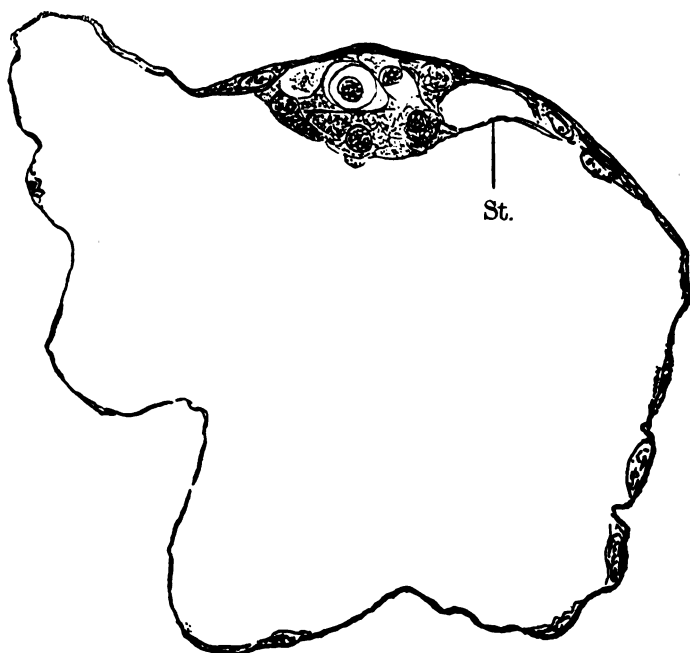


FIG. 5.—Vertical section through a blastocyst of the goat. Age, 9 days. The strand, St., seen in Fig. 2, is visible passing from the inner mass to the trophoblast.  $\times 400$ .

As viewed whole, the blastocyst, which measured 18 by 19 units, showed the germinal area as a rather oblong inner mass measuring 7 by 6 units, the longer axis being at right angles to the longer axis of the blastocyst. When seen from within, a very distinct strand was observed passing from one of the cells of the inner mass to the wall. This is seen quite easily on the section. (Fig. 5, St.) At one part of the edge of the inner mass the area seemed to pass more gradually into the blastocyst wall. On examination of the series of sections I find that there is only a doubtful differentiation into epiblast and hypoblast. (Fig. 5.) Very probably the separation is as suggested by the figure, but it is by no means certain. Fig. 5 represents the fourth section of the series and shows quite plainly the connecting strand of protoplasm referred to before and seen in Fig. 2.

Sections 3, 2 and 1 show a large cell which is either an epiblast cell occupying a gap in the trophoblast, or a trophoblast cell a great deal larger than is usual. (Fig. 6, a, b, c.) I can find no trace of a separate layer outside it. In, however, the previous stage there is certainly no trace of such a gap or hypertrophied cell; but this is no doubt the mergence mentioned above as perceptible in the whole specimen.

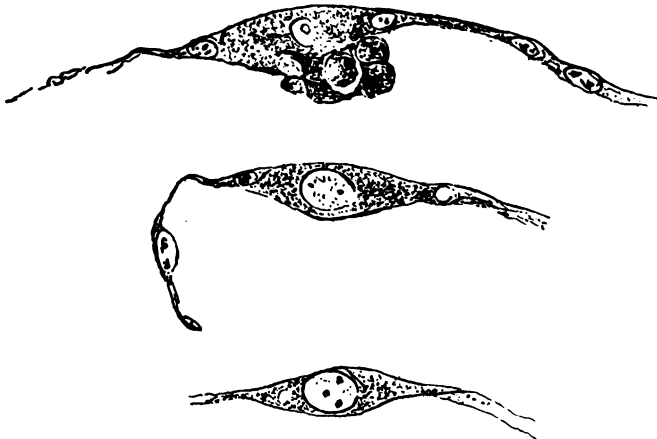


FIG. 6.—Three sections through the margin of the inner mass seen in Figs. 2 and 5.  $\times 400$ .

The sections in the other direction show about a similar degree of possible differentiation into epiblast and hypoblast, and in each case undoubtedly show an outer trophoblast covering layer, and do not differ greatly from the section drawn above (Fig. 5).

The second embryo obtained from this animal was larger, and measured 27.25 by 23.00 units, and was more elongated. The embryonal area was rather smaller than in the other specimens, and measured 5 by 6 units, the longitudinal axis lying, as before, at right angles to the longer axis of the blastocyst. When examined whole the inner mass showed a distinct inner contour which suggested a definite separation of epiblast and hypoblast. The wall trophoblast cells were much more attenuated than in the other specimen. No doubt it is a slightly more advanced embryo than its fellow. In section, however, the inner contour is not much more distinct, but in most of the sections the differentiation between epiblast and hypoblast may be determined with safety. (Fig. 7.) This corresponds to my Fig. 17 of the sheep.

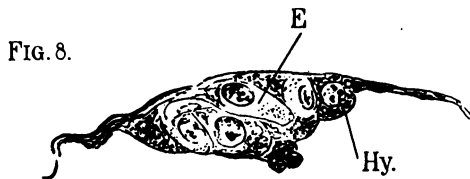
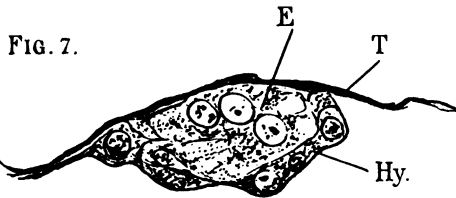


FIG. 7.—A section through the inner mass of Emb. 1 of Capra 4. This is the 5th of a series of 11. The trophoblast (T) is seen over the whole surface; the epiblast (E) and hypoblast (Hy.) are clearly distinguishable.  $\times 400$ .

FIG. 8.—The third section through the same inner mass. The epiblast (E) is exposed on the surface.  $\times 400$ .

The series of sections shows the embryonal area in eleven sections. Fig. 7 is the fifth of the series. The fourth to the eleventh certainly show the trophoblast extending over the whole epiblast, but in the second, and perhaps first and third, it appears to be absent (Fig. 8), thus rather supporting the view that the epiblast in both these cases is at the surface at one end—the more sloping end—of the embryonal area. In neither blastocyst does the hypoblast layer, if differentiated, extend beyond the edge of the embryonal area; that is to say, the wall of the blastocyst, except where the inner mass is placed, is monodermic. No trace of zona radiata occurs in either.

Capra 5. Age uncertain. One blastocyst was found considerably larger and more advanced than the former ones described, and corresponds in age to my Fig. 21 of the sheep, and Fig. 17 of Keibel's paper on the roe-deer. The specimen was fixed within six minutes of the death of the animal. This blastocyst, which was more elongated than the former ones, had become didermic as regards the upper half, the endoderm having been spread over the inner surface of the trophoblast to about the equator of the blastocyst, though forming only a network of protoplasm except close to the epiblast disc. The epiblast disc is much altered. It now shows signs of great activity, its cells are large, vacuolated, and arranged in columns radiating towards a centre on the outer surface, in a way similar to the corresponding stages in pig, sheep and deer. The nuclei are large and show mitotic figures, and are clearly differentiated from the nuclei of the hypoblast, which are small and darker. How the epiblast lies with reference to the trophoblast is a difficult matter to decide. In some sections there are undoubted trophoblast cells on the surface with dark nuclei. In other sections I think the trophoblast is wanting.

Fig. 9, which is the sixth of a series of fourteen, represents an interesting condition, in which there is some evidence of the next stage—the rise of the epiblast to the surface—being initiated by changes that occur in the trophoblast at one end of the embryonal area.

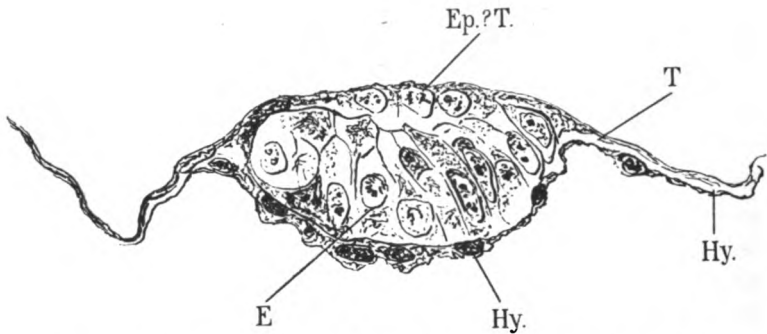


FIG. 9.—Transverse section through the embryonal area of an older specimen of the goat. E, Epiblast; Hy., Hypoblast; T, Trophoblast. Ep.?T., Cells of doubtful origin.  $\times 400$ .

In the pig, Weyssse,<sup>21</sup> Assheton<sup>3</sup>; in the roe-deer, Keibel,<sup>14</sup> in a less degree; and in the sheep, Assheton,<sup>4</sup> in a still less degree, the arrival of the epiblast to the surface is brought about by the arching inwards of the rapidly expanding epiblast plate and subsequent straightening out thereof, bringing about the rupture of the overlying trophoblast. The flattened plate then joins up round its edge with the torn edge of the trophoblast, and, completing the wall, takes its proper place upon the surface of the vesicle. In the oldest specimen of the goat there is, clearly enough, the thickened plate of large epiblast cells which, by their radial arrangement, suggest an arching comparable to the cases mentioned above; but if it never gets more than is here shown it does not amount to much. And I think the epiblast is already at the surface.

Now in the earlier stage (in *Capra* 4) the epiblast is either already at the surface at the end of the embryonal area (Fig. 6), or else changes have occurred in the trophoblast bringing about a return from the attenuated state of its cells to a condition of less stress, due presumably to a local relaxation of tension owing in some way to the modified arching of the epiblastic plate. It is, however, only a suggestion, as the material is far too scanty to enable one to form a decided opinion, but if there is some such relaxation, this might account for the accumulation of a few

trophoblast cells above the plate of epiblast, similar, for instance, to those which occur so clearly in the case of the pig.

Of such nature also may be the small cells in the later stage of the goat (Fig. 9) seen above the large epiblast cells, and not obviously covered by a trophoblast layer. They may be epiblast nuclei, but they are smaller than the majority of the epiblast nuclei, and they do not form part of the plate. In this section, and in others, there is certainly a more solid basal part, the actual epiblastic plate. There are in some sections near the edge of the disc undoubted trophoblast cells and nuclei on the surface. But what are these cells seen at Ep. ? T. in Fig. 9? No doubt they correspond to the upper smaller cells in Keibel's Figs. 18 or 20, or perhaps in 24A. But are they epiblastic or trophoblastic? If they are trophoblastic, then are we to assume that there is an incipient *träger* formation, such as occurs in a marked degree in *Mus* and *Cavia*? But they certainly resemble the epiblast cells more than the trophoblast. In the roe-deer, which seems to correspond very closely to this (*vide* Keibel's figures referred to above), they still more resemble epiblast. If we take them to be epiblastic, then we may regard them as being representative of a rudimentary true amnion, but one that is transitory, for the ultimate true amnion will be formed much later in a manner analogous to the formation of the Sauropsidan amnion, although it is probably not, strictly speaking, absolutely homologous to it (*vide* figures Assheton,<sup>2</sup> Pl. 18).

If this is the correct interpretation then, it perhaps points to the formation of the amnion as it occurs in *Cavia* as the more primitive Eutherian method, as advocated by Hubrecht and Van Beneden, though from rather different points of view. At least it is easier to conceive this condition to be a vestige rather than a rudiment. Whether this primitive Eutherian amnion is actually homologous to the Sauropsidan amnion and to the Prototherian and Metatherian amnion is debateable.

It seems to me probable that the Prototherian and Metatherian amnion is homologous to the Sauropsidan amnion; and that the ultimate amnion of *Capra* and other ungulates and many other Eutherians is certainly not strictly homologous to the amnion of



Sauropsida or Prototheria or Metatheria; and that this primitive—at least primitive as regards Eutheria—amnion, which is transitory in *Capra* and *Cervus*, more evident in some Insectivora and Cheiroptera and permanent in *Cavia* and probably Primates, may or may not be homologous to that of Prototheria, Metatheria and Sauropsida.

The alternative view is that the cells Ep. ? T. in Fig. 9 are trophoblastic and represent "träger" tissue rather than amnion; that is to say, the inner mass has a wad of trophoblast above the epiblast from an early period, which is a simpler explanation in some ways and can be adapted to all cases through the series from the guinea-pig through mouse, bat, mole, deer, pig, sheep, goat, ferret to rabbit and makes its appearance in gradually diminishing intensity in correlation with changed environment, of which the chief factors are size and character of the uterus, presence and varying persistence of zona radiata and other investments to the egg, such as a mucous or albumen layer laid on by uterus or Fallopian tube.

I am inclined to think that the observations on the goat itself, so far as they go, favour the former view, although the latter is quite defensible from a theoretical point of view.

#### SUMMARY ON CAPRA.

The result of these observations may be summed up thus: The ovum of the goat develops by the sixth day into a blastocyst, the characters of which closely resemble those of the sheep of about the same age, though the cavity of the blastocyst is more sharply defined. The blastocyst may be described as a vesicle with a thickened wall at one pole forming about two-thirds of the whole, and a thinner unilaminar wall forming the third part. As the blastocyst increases in size, the thicker pole is gradually thinned out, many cells of the thickened pole passing into and forming part of the unilaminar wall which increases rapidly in proportion to the multilaminar part until a typical blastodermic vesicle is formed, having a trophoblastic wall completely enclosing an inner mass of cells consisting of hypoblast, epiblast and perhaps some trophoblast, but not yet distinctly marked off from

— —

one another. A little later the epiblast becomes apparent as a mass occupying the centre of the inner mass. The cells of the epiblast are larger, more vacuolated, and lighter in colour than the rest. The embryonal area is slightly elongated and lies at right angles to the slightly elongated blastocyst. The epiblast then arrives at the surface by bursting its way through the trophoblast, in connection with which process the plate of epiblast becomes arched inwards, and the trophoblast ruptured, thus allowing the epiblast to take its place on the surface and become joined up to the trophoblast which holds it by its edge around the whole circumference. There is some slight suggestion that the trophoblast becomes thickened over the epiblastic plate during this process, giving rise to the few smaller cells which seem to lie in the trough of the plate. If they are thus of trophoblastic origin this thickening should be regarded as "träger"—if epiblastic, then as a vestigeal primitive Eutherian amnion. These alternations are discussed above.

#### HOMOLOGIES OF THE GERMINAL LAYERS OF MAMMALS.

Closely connected with this question is that of the homologies of the germinal layers.

The development of the egg of the pig is given as a type for the study of Eutherian segmentation and germ layer formation, because it does not lend itself to any particular theory of germ layer formation, but presents in a clear manner all the features which are generally accepted as non-controversial and typical of Eutherian development. The ovum of the pig contains food material in the form of oil, and passes very rapidly down the Fallopian tube, undergoing the first and second cell divisions before arriving in the uterus. There is no addition of albumen or other investment outside the zona radiata. The egg segments as shown in the accompanying figures, and results in a morula, the segmentation spheres varying much in size in different specimens. This completes the segmentation stage, and the solid morula is converted into the blastocyst by the infiltration of fluid and its collection into vacuoles which run together and so give rise to the large fluid space which may be intracellular in its first

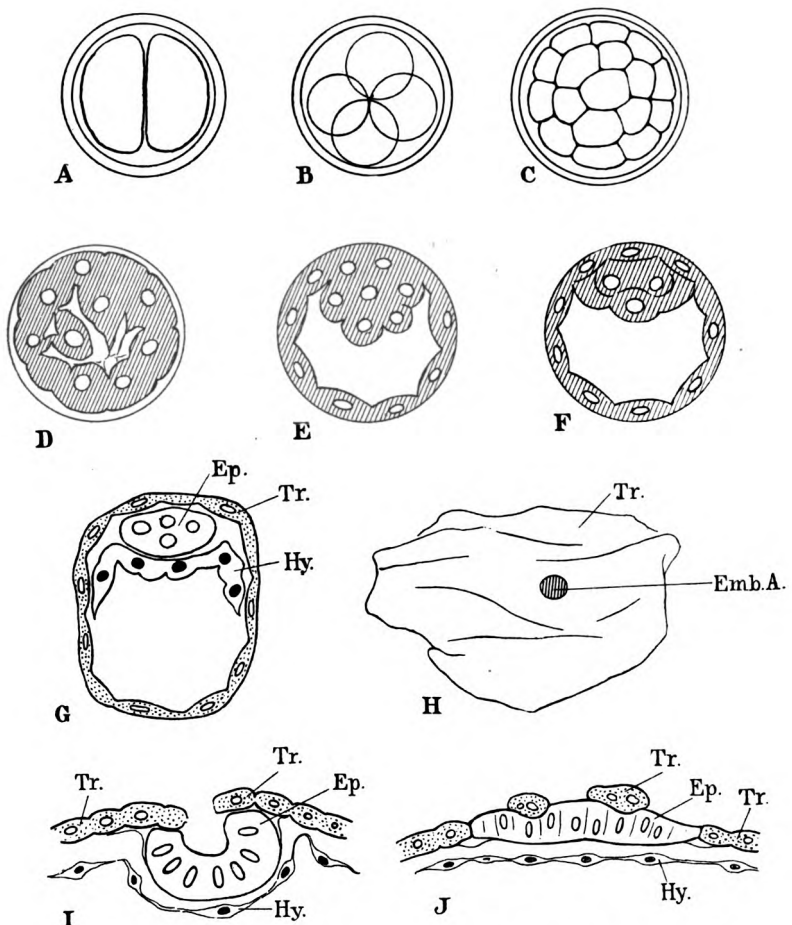


FIG. 10.—Diagrams to illustrate the generally accepted course of development of a Eutherian Mammal. Emb. A. Embryonal area; Ep. Epiblast; Hy. Hypoblast; Tr. Trophoblast; Tr. Degenerating Fragments of Trophoblast.

origin, but becomes intercellular as it becomes more and more distended. This fluid space becomes eventually the cavity of the gut, and so may as well be termed archenteron from the first, being homologous to the sub-germinal cavity of reptiles and birds. It arises eccentrically, and so the wall of the blastocyst is thicker

at one pole than elsewhere (E, Fig. 10). As the blastocyst expands, some of the cells of the thickened pole remain within, projecting into the cavity as an inner mass, but always adhere at one point to the wall, which elsewhere is unilaminar, and is known now as the trophoblast owing to the fact that it is this layer of cells which will eventually play the chief part in procuring nutriment for the embryo from the uterine walls.

Soon the inner mass becomes differentiated into a central group of cells (Ep. G, Fig. 10), and a lower layer lining its inner surface, which latter becomes carried or spreads over the inner surface of the outer wall as the whole vesicle expands (Hy. G, Fig. 10). The central group Ep. remains inert for several days, then begins to grow rapidly and forms a plate of cells, which becomes arched inwards and breaks its way through the outer wall and so comes to the surface (I, Fig. 10) tearing and breaking up the over-lying outer wall-cells which are cast off and lost, and is known as the embryonal area. Thus, this embryonal area, which is disc-like, consisting of cells with large nuclei, has appeared on the surface, having been derived from a mass which a day or two previously had been enclosed within the wall of the vesicle. I would now lay special stress upon two facts, namely, (1) the marked distinctness between the cells composing the disc and those of the trophoblast with which it is now continuous (J, Fig. 10); (2) the rejection of the trophoblast cells which formerly covered it. There is no ultimate tendency to a fusion or of any further use being made of these pieces of torn off trophoblast.

We can now identify three quite distinct parts, and can predict the fate of each. Firstly (1). *The trophoblast* which forms the outer wall of the vesicle, except for a small disc, the embryonal area, which it holds by its edge. This layer, the trophoblast, takes part in the formation of the placenta and the false amnion and some of the true amnion. No portion remains in the adult. Secondly (2). *The embryonal area* which gives rise to all the *ectodermal* structures of the embryo and adult and part of the amnion, and the ectoderm of the umbilical cord, and to the growing point (primitive streak) from which a large part (deutero-genetic) of the embryo is formed. Thirdly (3). *The inner layer*

which now lines nearly the whole of the inside of the blastodermic vesicle. This gives rise to the gut and the derivatives thereof and protogenetic mesoblast and, so forms a large part of the adult. It also takes part in the formation of purely embryonic structures, the yolk sac and allantois with the splanchnopleure covering them, which are thrown off at birth. It can be called the hypoblast.

The method of curvature by which the embryonal area, *i.e.*, epiblast, breaks through the trophoblast and comes to the surface is characteristic of many mammals, though not of all. In the closely-allied genus *Cervus* (roe-deer) it is more marked (Keibel<sup>14</sup>), while in *Ovis* and *Capra* it is less distinct even than in the pig. Looking beyond the ungulates we see complete series of forms which diverge in opposite directions—one towards an intensification of the process culminating in *Cavia*, the other towards a complete absence of it, as represented by *Lepus*.

	Small trace of entypy		<i>Cavia</i>	Complete entypy.
			<i>Mus</i>	
			<i>Arvicola</i>	
			<i>Vespertilio</i>	
			<i>Pteropus</i>	
			<i>Erinaceus</i>	
			<i>Talpa</i>	
			<i>Tupaia</i>	
			<i>Tarsius</i>	
			<i>Cervus</i>	
		← <i>Sus</i> →		
towards	<i>Lepus</i>			towards
	<i>Sorex</i>			
	<i>Canis</i>			
	<i>Putorius</i>			
	<i>Capra</i>			
	<i>Ovis</i>			

At first sight the extremes appear to be very different. The condition in the rabbit resembles more closely than any mammal the conditions of the bird's development, while in the guinea-pig we have the phenomenon known as inversion of layers, or perhaps better expressed by the phrase entypy of the germinal area. A little consideration of this series, however, may help to show that the differences are neither great nor important.\* In the development of all these forms there are *certain features which are common to all*. Thus, all arrive at a solid morula stage as the result of segmentation, which by infiltration of fluids

\* Plate xvi. in Selenka's *Entwicklungsgeschichte der Thiere*, and Plate xviii. in my paper on the Sheep, *Quart. Journ. of Micro. Sci.*, Vol. xli., may prove useful references.

becomes hollowed out into the blastodermic vesicle having a wall thin over the greater part but thickened at one pole. At this pole eventually an inner mass is separated off. This in all cases contains the cells that will give rise to the whole of the adult animal. In all cases these cells are sooner or later differentiated into two layers, which from that time are also sharply differentiated from the trophoblast and from the epiblast and hypoblast respectively.

The differences are :—(1) That in some the inner mass contains also a certain number of trophoblast cells—or in other words, the trophoblast is, or becomes in certain cases, thickened over the inner mass slightly in pig or tupaia, more in mole, deer, bat, and very greatly in mus, cavia, etc. (2) This results in another difference, namely, that where accentuated, as in bat or mouse, the inner mass never comes to the surface as in the other cases; and in extreme instances it is accompanied by a totally different mode of formation of the amnion (*Cavia* and perhaps *Primates*).

How slight and unimportant these differences are from a morphological point of view is indicated by the fact that the rabbit and the guinea-pig, closely allied animals, are at the extreme and different ends of the series.

A close study of the development shows that in reality there is the same physiological centre of activity at work. The centre of activity, which gives rise to the heaping up of the "träger" of *Mus* or *Cavia*, is present in a nearly corresponding position in the rabbit, but owing to certain external causes, such as the persistence of a tough outer investment, the albumen layer, a totally different form is assumed, leading ultimately to a different mode of amnion formation. According to this view the cells Ep. ? T of Fig. 9 *Capra* would be trophoblastic rather than epiblastic, but I do not think the evidence is sufficient in this instance to enable one to decide.

In comparing the early stages of Eutherian development with those of other vertebrates, one is struck with certain peculiarities. Throughout this series, there are three features which are characteristic of and peculiar to Eutherian development:—(1) The inclusion of the embryonic knob (*i.e.*, the cells which give rise to

the adult animal) within a vesicle of protective and trophic cells ; (2) The attempts on the part of this embryonic knob to break through the walls of this protective and trophic vesicle and to come to the surface ; (3) The rejection of the trophic cells by the cells of the embryonic knob (embryonal area). What explanation can we give of these differences ? In other words what *are* the homologies of the germinal layers of mammals ?

At the present time the doctrine of the homology of the germinal layers—*i.e.*, of the ectoderm to the ectoderm of all animals, and of the endoderm to the endoderm of all other animals—is less strongly insisted upon than it was twenty years ago. Some zoologists would abandon it altogether as useless. If I may venture to express an opinion, I would say that, however great may be the undoubted difficulties in the way of the full acceptance of the theory, the difficulties of totally rejecting it seem to me to be infinitely greater ; for, although for convenience we speak of, for instance, the embryo chick as something apart from the membranes from which it seems to grow, yet these membranes, the germ layers, are just as much part of the embryo as the legs or wings are parts of the adult bird, and we *must* expect homologies to exist in each case. The germ layer theory occupies a position very similar to the theory of recapitulation. A firm basis of truth underlies each, and to me it seems that if we reject these theories the word homology has no meaning, and we must reject also the theory of evolution.

Although the recapitulation theory postulates a fundamental general principle of zoology, yet no animal accurately recapitulates its own ancestral history. That is impossible—and some recapitulate hardly any part of it. So, also, although the germ layer theory may be regarded as a fundamental general principle of embryology, yet it is possible that in some cases modifications have occurred in the later history of the species which have obliterated the original course of early events. If we admit the possibility of such modifications, then clearly the origin of an organ from the corresponding germinal layer in two animals may not be of itself an absolute proof of homology. But, even if we admit that similarity of origin of parts in ontogeny does not

afford an infallible criterion of the homology of these organs, yet it offers evidence fully as important as that afforded by any other test.

In discussing the homologies of the germ layers of Eutherian mammals, one would naturally turn to the development of the Monotremes and Marsupials for the answer. Unfortunately, very little is known of the early stages in the development of the Monotreme. Caldwell has published almost nothing; Semon only a few segmentation stages from which we can derive but little help; Wilson and Hill have recently published a very important paper in which they describe later stages where certain structures are found resembling the conditions of a reptilian egg, together with early segmentation stages from which, however, we gain very little help towards the elucidation of Eutherian development.

Of the Marsupials, Selenka alone gives any real information; but so difficult is it to interpret in terms of the Eutherian development, that all I can do is to point out the differences, and to conclude that the differences between the development of the Eutherian and that of Metatheria and Prototheria are fundamental.\* The differences are:—(1) It seems to be very uncertain whether the zona radiata, so characteristic an investment to the Eutherian ovum, is present in the Metatheria. (2) In the stage in which four segments occur, these four segments lie in the Metatheria, all in one plane, as they do in the corresponding stage of segmentation in such eggs as those of *Amphioxus* and *Amphibians*, and unlike the Eutherian condition in which they invariably lie, so that one pair is at right angles to the other pair. To this fact is probably due:—(3) The fact that the result of segmentation in the Metatheria is a hollow "blastula" (?), as it is in *Amphioxus* and *Amphibians*, and not a solid morula, as it always is in Eutheria; perhaps a difference of not very wide significance, but one of great importance within the limits of the class *Mammalia*. Whether this hollow sphere is really comparable to the blastula is another matter, and one which cannot be profitably discussed until further knowledge has been obtained. (4) There is no

\* *Vide* Note on Hill's recent work, page 236.



layer that can with much justification be described as trophoblast, that is to say morphologically; but the wall of the vesicle is clearly trophic, as shown by Caldwell,<sup>8</sup> Hill,<sup>9,10</sup> Osborne,<sup>16</sup> Semon,<sup>20</sup> though Hubrecht<sup>12</sup> interprets Selenka's ectoderm in this sense. Since the Monotremes and Marsupials at present afford us little assistance, we are obliged to obtain what hint we can from a more exact study of Eutherian eggs. (*Vide* note on page 236 with reference to Hill's work on *Dasyurus*.)

Van Beneden, in 1875 and 1880, published his classical papers on the segmentation of the ovum of the rabbit. His results are known to all; figures drawn from his description or copied from his drawing are in almost every text-book. He believed that he could distinguish a differentiation of blastomeres into smaller blastomeres, the descendants of one of the two segments resulting from the first division of the ovum, and larger blastomeres, the descendants of the other. The smaller ones he described as enveloping the larger ones, which phenomenon he described as a gastrulation by epibole. The aperture left just before complete envelopment he called blastopore, and the outer layer ectoderm and inner mass endoderm; and later, when this inner mass separates into two layers, he regarded the innermost layer as endoderm, the middle layer as mesoderm. This view, however, was shown conclusively afterwards by Kolliker, Heape and others to be untenable, and was abandoned by Van Beneden himself, though again resuscitated in 1896, by Duval, to account for similar appearances in the bat. There is, however, no doubt that in the rabbit the middle layer comes to the surface as in the pig, though in a less obvious manner, and without arching, and forms the embryonal area from which the ectoderm of the embryo is formed.

A few years ago Van Beneden returned to this problem, and published in 1899 an important paper upon the formation of the germinal layers in the Cheiroptera. He upheld his former view as regards the differentiation into two kinds of blastomeres, and the envelopment of the one set by the other, but no longer regarded this as a case of epibolic gastrulation. He guards against the assumption that every specimen shows evidence of differentiation

of cells suggesting an epibole, for many certainly do not, a circumstance which agreed with my own observations on the sheep.

Van Beneden's explanation of the early epibole is this: He holds that mammals are descended from animals having large-yolked meroblastic eggs, like the other Amniotes and the Monotremes, but that owing to the evolution of the placental nourishment they have lost the yolk. He sees in this epibole the

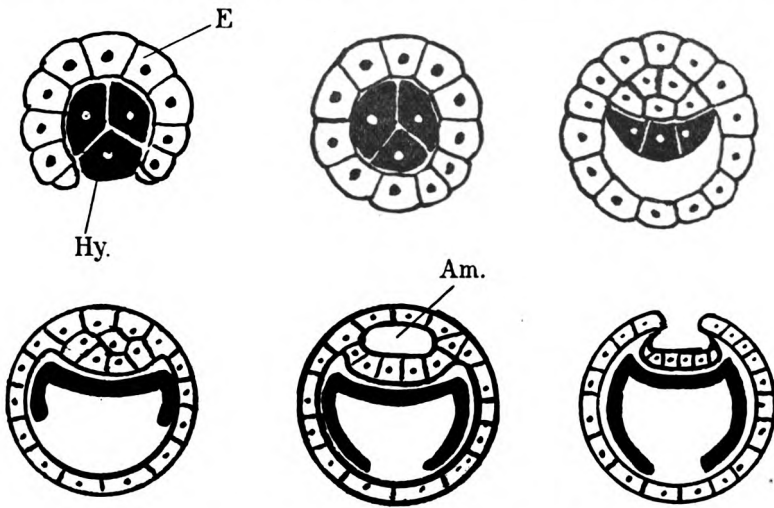


FIG. 11.—Epibols and development of mammalian egg according to the interpretation of Van Beneden. The trophoblast is therefore epiblastic, and the epibols represent the growth of the epiblastic edge of the blastoderm over the yolk. E., epiblast; Hy., hypoblast; Am., amniotic cavity.

process of envelopment of the yolk sac by the advancing edge of the epiblast, such as proceeds slowly during the first days of development of the bird's egg. It is not a process of gastrulation; therefore, according to him, the trophoblast is the homologue of the so-called extra-embryonic epiblast of the reptilian or avine egg. The embryonal area he regards as inverted more or less in all mammals, as suggested originally by Minot.

There seems to me to be much to be said in favour of this view, but there are certain objections:—(1) It does not account

for the marked difference that occurs between the character of the trophoblast cells and epiblast cells ; (2) It does not account for the rejection of the trophoblast cells by the epiblast of the embryonal area, a rejection we can well understand if the trophoblast cells are really hypoblastic in origin ; (3) Van Beneden is also a little inconsistent, for in his former papers on the rabbit he shows that the epibole is in the opposite direction to that required by his newer hypothesis. In 1880, in his description of the rabbit, he describes the epibole as occurring in such a way as to place the inner mass at the point where the enveloping rim coalesces (*vide* Van Beneden,<sup>5</sup> Fig. 7, Fig. 5<sup>111</sup>), and marks the spot where the embryonal area will eventually be.

This I believe to be quite correct, and accords with what I find in the sheep's segmentation. But Van Beneden's last view surely requires that the epibole, which he regards as the enveloping epiblast of the blastoderm, should be in the opposite direction, so that the coalescing rim should be on the ab-embryonic pole, as in the Sauropsidan eggs.

Hubrecht takes an entirely opposite view. He maintains that mammals are more closely related to amphibia than to reptiles. He sees no evidence in mammalian development which necessarily implies descent from ancestors with large meroblastic eggs, such as the Sauropsida. He believes the mammals are descended from animals with small yolkless eggs, and that the blastodermic vesicle is a trophic vesicle, a special embryonic organ developed in correlation with a uterine gestation, just as Willey<sup>22</sup> argues for *Peripatus Novæ Britanniae*, and that the richly-yolked egg of the *Prototheria* is secondary. The trophoblast he regards as analogous to protective layers, such as are found in the *Pilidium* larva or in *Cunina*, or *Zoogonus*, etc., and homologous to the epidermic layer of epiblast in certain *Ithyopsida*. He would derive mammals directly from the amphibia, and the trophoblast from the epidermic layer of the epiblast, into which the epiblast of *Anura* embryos is divided. This he imagines to have become split off and to have given rise to the amnion of mammals and of the Sauropsida as well. He points to a layer of cells which has been detected in some Sauropsidan embryos outside the epiblast as

being the homologue of the trophoblast; for instance, by Mehnert in the duck and by Schauinsland in *Sphenodon*.

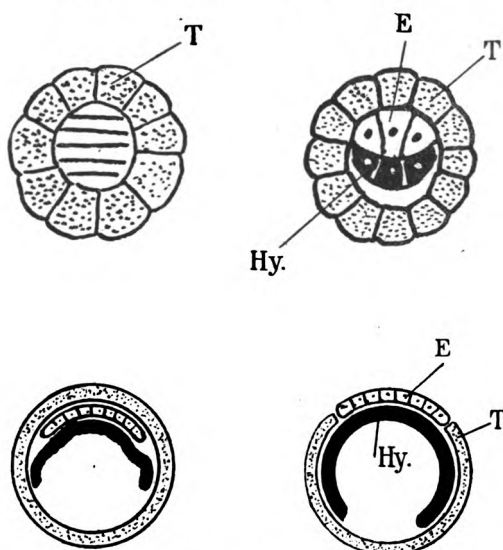


FIG. 12.—Diagrams to illustrate development of Eutherian egg according to Hubrecht. The dotted layer trophoblast is a special layer like the protection layer of teleosts, and is separated off before epiblast and hypoblast are differentiated. The epibols seen in sheep or bats' egg would be interpreted as a growing round of the trophoblast over the undifferentiated embryonic mass.

It is extremely difficult to believe that the remarkably close resemblance between the embryo of the Sauropsida and the embryo of the Eutherian mammal and its membranes in all its stages is mere coincidence. Hubrecht's references to protective or nutritive membranes, such as those of *Peripatus*, *Pilidium*, *Zoogonus*, are after all only analogies. But to the Anura he distinctly appeals for homology; but here there seems to be considerable difficulty.

It is very evident how different in the pig the trophoblast cells are to the epiblast, and how the latter rejects the former. In the Anura there is certainly a separation of the epiblast into two layers; but a closer examination produces no evidence of the outer being either specially protective or nutritive. The outer

becomes the supporting cells or neuroglia of the central nervous system, the inner the nerve cells. It is really an early separation into what His called spongioblast tissue and neuroblast tissue.

Van Beneden will have none of this theory; he says Hubrecht's hypothesis encounters insurmountable difficulties, both morphological and physiological. It leaves unexplained the presence in placental mammals of an umbilical vesicle and a host of characters common to all Amniotes and distinctive of those animals. There can be no doubt at all that this theory of the trophoblast is one that, both from a morphological and physiological standpoint, has a supreme importance; but seeing that protective envelopes develop when necessity calls for them in such diverse groups of animals as Vertebrates, Insects, Echinoderms, Nemertines, Platyhelminthes, etc., where a general homology can hardly be suggested, one may legitimately doubt whether all within one phylum must be homologous.

I think it will be admitted that the case of the Anura (where it is, by the way, apparently particularly well formed) must be dropped. Still that leaves us with the trophic or protective layers of the Eutheria, Sauropsida (though here it is vestigial) and the Teleosts.

If, then, these layers alluded to by Hubrecht in these classes of Chordates are really homologous, it does certainly present the evolution of the trophoblast as a very ancient event; and in that case we need not be surprised that in the Eutherian mammal it differentiates at a very early stage, and we can—if other facts offer no obstacle—regard the epibole of rabbits', bats', sheep's, etc., eggs as the separation of, and surrounding of, the germ by a well-developed trophic layer. I am very far from disbelieving the theory, but I think the facts of Eutherian development are explained better by a theory I will allude to in a later paragraph. The chief objections to Hubrecht's theory seem to me to be:— (1) It does not account satisfactorily for the early epibole of the Eutherian segmenting ovum. (2) It offers no explanation of Entypy or of the rejection of the trophoblast cells by the epiblast. (3) It disregards the Sauropsidan affinities of mammals and those especially of the Prototheria. (4) In spite of Hubrecht's attempt,

it is difficult to regard the Metatheria as offering any support to the theory.

There is another interpretation which I once suggested, based upon the appearance of some segmenting eggs of the sheep, and on the hypothesis that mammals are descended from ancestors with meroblastic eggs like those of living Sauropsida, and which owes much also to the theoretical conclusions of Minot and Robinson (*vide* Assheton<sup>2</sup>). According to this explanation there is an overgrowth of some cells at an early stage, but these overgrowing cells are hypoblastic—or, speaking more accurately, yolk cells. The epiblast thus becomes completely covered in and remains an inactive mass until the blastocyst has attained a size suitable for its further development upon the old meroblastic egg plan. When that stage is reached, the epiblast becomes more active, and by various means tends to work its way to the surface. In blastocysts which become early imbedded, it never actually reaches the surface, being by this time completely buried by an accumulation of rapidly multiplying trophic cells which according

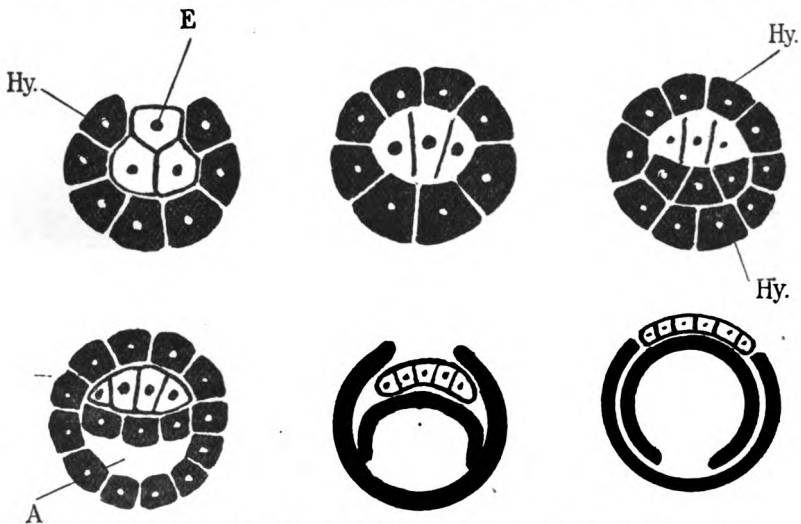


FIG. 13 (after Assheton).—Diagrams to show hypoblastic theory of the trophoblast founded on development of sheep. The epibole is an overflowing of hypoblast, or yolk cells, whereby the epiblast is temporarily covered. It is peculiar to Eutherian mammals. A, archenteron; E, epiblast; Hy., hypoblast.

to this view are hypoblastic or yolk cells. This is the case in forms like *Cavia*, *Mus*, and probably *Man*. This outer layer of originally yolk cells is Hubrecht's trophoblast.

It is supposed that in the proto-Eutherian, during the loss of yolk and therefore great diminution in size of the egg, the epiblast had to lag behind in its development more and more until such time as the infiltration of fluid caused the sub-germinal cavity to swell up large enough for the development of the more bulky parts along the old ancestral lines. The result was that the yolk cells have overflowed and imbedded the inert epiblast knob. The cavity of the blastocyst is therefore regarded as the sub-germinal cavity of the meroblastic egg of the Sauropsida and is the archenteron. Its formation constitutes the sole process of gastrulation in Eutherian mammals—there is no blastopore. According to this explanation there has been complete continuity of function. The sub-germinal cavity formed in the meroblastic egg as a space between yolk cells has continued its mode of formation and its tendency to swell up by infiltration of fluids, and the yolk cells have retained their original function of providing food for the nourishment of the rest of the embryo. On this theory gastrulation commences at the moment of the appearance of the cavity of the blastocyst which is to be regarded as archenteron and finishes when the hypoblast is clearly defined.

There is an apparent break now—a long period of slowing down—during which the conditions pertaining to the old ancestral large yolked egg are being regained. These conditions are chiefly the production of a sufficient size, and, in most cases, the rising to the surface of the plate of epiblast. I say apparent, because I do not suppose that it is absolute, but it is a period so much drawn out that it almost constitutes a break between what I call protogenesis and deutero-genesis (Keibel's first and second period of gastrulation), for I regard protogenetic activity alone as concerned in gastrulation. Deutero-genesis is growth in length of the already gastrulated embryo, a distinction which, to my mind, is of real importance.

Such are three of the interpretations suggested to account for the observed facts of this early phase of Eutherian mammalian

development. Briefly the problem is this: there is in all Eutherian mammals at an early stage an enclosure of the embryonic rudiment, which, in the majority of cases, breaks its way out and appears on the surface and assumes a condition similar to that of the embryonic rudiment of the meroblastic egg of other Amniota. This covering layer, which forms no part of the adult animal, is in many instances differentiated at an exceedingly early period of development. In certain species there is some evidence that this layer develops from a group of cells which at first do not surround the embryonic rudiment, but grow round it subsequently. How has this layer arisen in the evolution of Eutherian mammals? Can it be said to be homologous to any part of the Sauropsidan embryonic membranes?

Hubrecht attempts to solve the problem by deriving the trophoblast and amnion from pre-amniote tissues, comparing them morphologically with the outer layer of ectoderm of Anura. Van Beneden who, like Balfour, derives the Eutherian condition from a meroblastic egg of the Sauropsidan type, regards the enveloping layer—the trophoblast—as the homologue of the extra embryonic ectoderm.

I would certainly agree with Van Beneden, Balfour, Minot and others in believing that mammals are descended from ancestors having large yolked eggs of the Sauropsidan type, but I still think that the account I gave of the trophoblast being derived from yolk cells, a theory first advanced by Minot, and first supported by actual observation by myself in my work on the sheep, and adopted with modifications, is an hypothesis which best fits in with the observed facts of mammalian development and with physiological necessities which must have occurred in the change from a yolk nutrition to one derived from the walls of the uterus.

NOTE ON HILL AND WILSON'S WORK ON PROTOTHERIA AND  
METATHERIA.

The recent work of Wilson and Hill,<sup>23</sup> and of Hill,<sup>11</sup> confirm the opinion that earlier stages of the development of Monotremes and Marsupials *differ* very considerably from the Eutherian



type, this difference being chiefly the fact that in these groups there is no suggestion of any envelopment of the epiblast (or epiblast and hypoblast) by a trophoblast, that is to say, entypy is a strictly Eutherian character.

Although the earliest stages of the Monotreme (Prototheria) are still imperfectly known, still we can say safely that there is no special trophoblastic layer. The epiblast quickly surrounds the yolk mass as it does more leisurely in reptiles and birds. In the Marsupials (Metatheria), however, there does seem to be a separation of trophoblast, but it never overflows, so to speak, the lethargic epiblast as I believe it does in all Eutherians.

Hill<sup>11</sup> has quite recently described the early stages of the development of the Marsupial *Dasyurus viverrinus* at a meeting of the British Association in Dublin. His account emphasises the fundamental difference between the segmentation of the Metatherian and Eutherian ovum.

The egg segments so as to form not a solid morula but a pair of rings, which may be said to occupy an equatorial position within the egg membrane. One of these spreads towards one pole—the upper pole—and is made up of smaller less yolk-bearing segments, the other spreads towards the other or lower pole and is formed of segments richer in yolk. Thus a closed unilaminar vesicle is formed comparable to the blastocyst of an Eutherian. From the products of the upper ring the definitive epiblast and hypoblast is formed, and is to be regarded as the equivalent of the embryonic knob of the Eutherian, *e.g.*, inner mass of pig blastocyst of five days; the other Hill regard as the homologue of the trophoblast, and forms the greater part of the general wall of the blastocyst as in Eutheria. Hill says the trophoblast is ectoderm. I cannot see why it should be called ectoderm more than endoderm. For my part I would rather regard it as either endodermal or at least non-differentiated yolk cells, comparable to the germinal wall-cells of Sauropsida. Hill's objection to this view is perhaps that he regards a curious non-nucleated part of the unsegmented egg which he describes as a delicate reticulum with fluid-filled meshes, and which is separated off prior to the commencement of cleavage, as representing the original yolk mass.

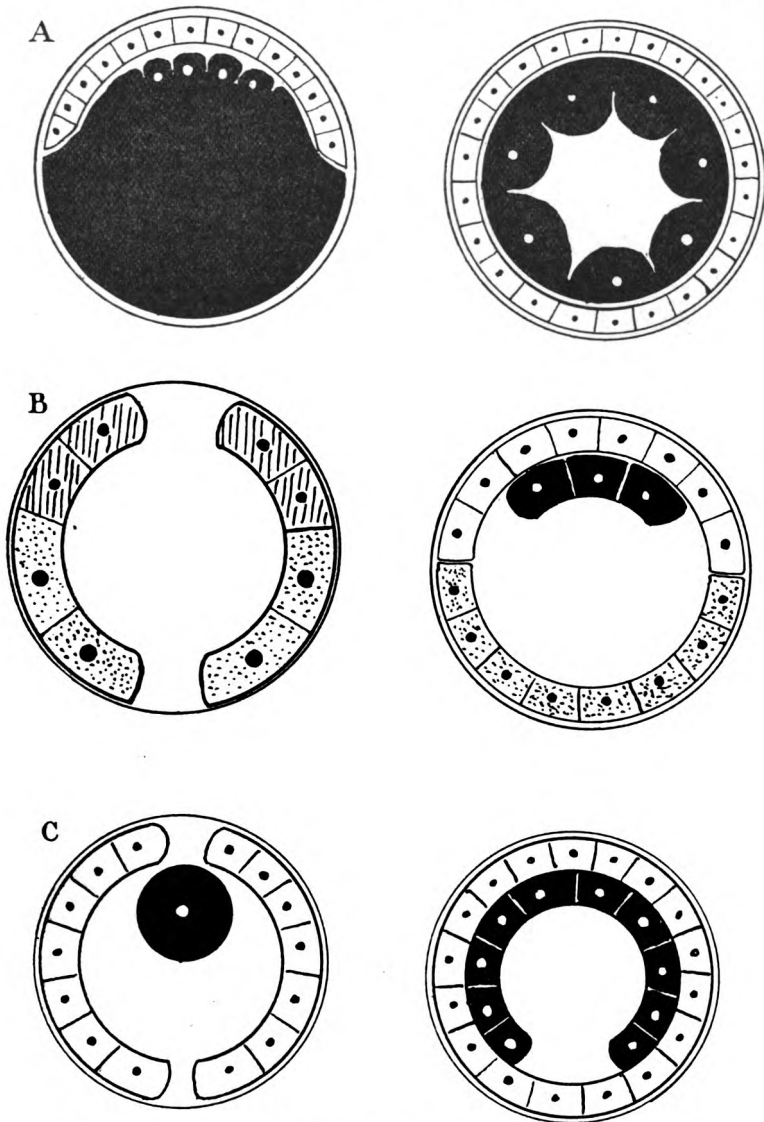


FIG. 14.—Diagrams to show the formation of the blastocyst in:—  
A, Prototheria after Caldwell, Semon, and Hill and Wilson's description; B, Metatheria after Hill's description of *Dasyurus*; C, Metatheria, after Selenka's description of the opossum.

White = epiblast; black = hypoblast and yolk; dotted area = trophoblast; shaded area = embryonic knob.

I am not quite clear from his description of the exact position of this mass. It would appear to be on the upper pole, therefore above the future ectoderm, in which case it is difficult to believe that this represents the yolk mass of lower vertebrates. If, however, it is on the lower pole, *i.e.*, on the side of the cells, which, he says, form the trophoblast, then it would seem to support rather than disprove the contention that the trophoblast and endoderm are of common origin.

Hill's work seems to me to support very clearly the theory that there is an early separation of trophoblast from other layers, but that whereas, in the Eutheria, this separated mass envelops the ectoderm for a while lethargic (or ectoderm and endoderm) causing the phenomenon of entypy, in the metatheria this overflowing or temporary overgrowth does not occur. Personally, I believe the sheep specimens described by me in 1898, go a long way to prove that this trophoblast is of endodermic or yolk cell origin rather than of ectoblastic origin, and explains in a very simple way with physiological continuity how the Eutherian peculiarities of development have arisen from the Sauropsidan type.

Fig. 14 B represents Hill's interpretation of *Dasyurus*, the dotted area being his ectoblastic trophoblast. I should like to interpret it as of hypoblastic in yolk cell origin and colour it black and compare it with my diagram above Fig. 13 by assuming that in metatheria there is no overgrowth of the epiblast cells, therefore no entypy, a condition correlated with the hollow blastula instead of solid morula form of the segmented egg.

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LIST  
OF  
GENTLEMEN EDUCATED AT GUY'S HOSPITAL  
WHO HAVE PASSED THE  
EXAMINATIONS OF THE SEVERAL UNIVERSITIES, COLLEGES,  
&c., &c.,  
IN THE YEAR 1907.

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**University of London.**

*Examination for the Degree of Doctor of Medicine.*

Branch I.—*Medicine.*

C. E. Iredell.		J. R. Steinhaeuser
B. A. Richmond		(Qualified for Gold Medal).
(Gold Medal).		R. O. Williams.

Branch IV.—*Midwifery and Diseases of Women.*

E. Bellingham Smith.		F. T. H. Wood.
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Branch V.—*State Medicine.*

M. de L. Robinson.

*Examination for the Degree of Master in Surgery.*

T. B. Layton (Gold Medal).

*Examination for the Degree of Bachelor of Surgery.*

E. C. B. Ibotson.

*Examination for the M.B., B.S. Degrees.*

May.

*Obtained Honours.*

W. H. Miller (Distinguished in Surgery).

Pass.

G. F. E. Allison.		G. Hamilton.		H. S. Knight.
K. H. Digby.		F. P. Hughes.		H. Joste Smith.

Supplementary Pass List.

Group II.—*Surgery, Midwifery, and Diseases of Women.*

T. E. Ashdown Carr.	E. L. R. Norton.
C. C. A. de Villiers.	R. J. Russell.

October.

Pass.

S. H. C. Air.	T. E. Ashdown Carr.	J. G. Phillips.
E. Alban.	C. C. A. de Villiers.	R. J. Reynolds.

Supplementary Pass List.

Group I.—*Medicine, Pathology, Forensic Medicine and Hygiene.*

C. A. Basker.

Group II.—*Surgery, Midwifery, and Diseases of Women.*

G. N. Bartlett.	J. B. Martin.	H. Stott.
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*Intermediate Examination in Medicine.*

January.

M. M. Adams.	C. H. Crump.	J. L. Johnston.
J. Lee Atkinson.	E. L. Elliott.	*G. H. Peall.
S. H. Brook.	A. L. Fitzmaurice.	J. R. Perdrau.
A. H. G. Burton.	G. F. Haycraft.	N. A. D. Sharp.
	W. E. Williams.	

\* *Distinguished in Anatomy.*

July.

R. P. Ballard.	J. B. Dunning.	G. R. Hind.
W. H. Catto.	M. A. E. Duvivier.	G. Maxted.
†‡A. Neville Cox.	H. Gardiner.	D. A. Mitchell.
G. Dunderdale.	W. L. Hibbert.	†T. D. M. Stout.

† *Distinguished in Anatomy.*

‡ *Distinguished in Pharmacology.*

*Preliminary Scientific Examination.*

January.

Part II.—*Organic Chemistry.*

J. A. Edmond.	P. Hirschbein.	A. H. Todd.
W. E. Fox.	P. Smith.	A. D. Vazquez.
	D. H. Wood.	

Part I.—*Inorganic Chemistry and Experimental Physics.*

(b) C. Aldis.	(b) T. E. Roberts.
(b) F. C. Hunot.	M. Scott.

*Inorganic Chemistry and Biology.*

(p) G. Covell.

*Inorganic Chemistry only.*

(pb) E. A. Barker.	(pb) V. Glendining.	(pb) L. B. Stringer.
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*Experimental Physics only.*

F. D. Annesley.		(cb) S. Wilson.
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*Biology only.*

(cp) H. Archer.		G. E. Genge Andrews.		(cp) J. M. Joly.
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(b) *Has already passed in Biology.*

(c) *Has already passed in Inorganic Chemistry.*

(p) *Has already passed in Experimental Physics.*

**University of Oxford.**

*Second M.B. Examination.*

Forensic Medicine and Hygiene.

C. G. Douglas.		O. G. F. Lunn.		N. Flower.
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Medicine, Surgery, and Midwifery.

R. Evans.		O. G. F. Lunn.		C. G. Douglas.
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**University of Cambridge.**

*Degree of Doctor of Medicine.*

C. R. Howard.		G. W. de P. Nicholson.
---------------	--	------------------------

*Third Examination for the Medical and Surgical Degrees.*

Part II.

H. B. Carlyll.		C. W. Greene.		C. W. Ponder.
R. G. Chase.		E. B. Hinde.		J. W. Ryffel.
A. T. Densham.		B. H. Palmer.		C. B. Ticehurst.
		R. R. Walker.		

Part I.

W. T. Chaning-Pearce.		J. H. Ryffel.		T. N. Wood.
C. E. M. Jones.		J. Walker.		C. S. E. Wright.
R. P. M. Roberts.		W. E. Wallis.		

*Diploma of Public Health.*

W. Gibson Parker.		M. de L. Robinson.
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**University of Durham.**

*Degree of Doctor in Medicine.*

Alan A. Smith.

*Examination for the Degree of Doctor in Medicine for  
Practitioners of Fifteen Years' standing.*

H. J. Roberts.

*Degrees of Bachelor in Medicine and Bachelor in Surgery  
and Bachelor in Surgery.*

E. P. H. Joynt.

|                      H. F. Joynt.

*Third Examination for the Degrees of Bachelor in Medicine  
and Bachelor in Surgery.*

H. C. W. Allott.  
L. W. Evans.

|                      R. C. H. Francis.  
A. C. Greene.

|                      E. P. L. Hughes.

*Second Examination for the Degrees of Bachelor in Medicine  
and Bachelor in Surgery.*

H. C. W. Allott.

|                      W. Reynolds.

*First Examination for the Degrees of Bachelor in Medicine  
and Bachelor in Surgery.*

**Entire Examination.**

H. F. Stephens.

*Chemistry and Physics.*

O. S. Norton.

---

**Royal College of Physicians of London.**

*Elected to the Fellowship.*

Herbert S. French.

*Examined for the Membership.*

H. C. Corry Mann.

*Final Examination for the Licence.*

January.

G. F. E. Allison	C. E. M. Jones	R. J. Reynolds
K. H. Digby	W. P. H. Munden	J. T. Smalley
H. G. Gibson	J. E. Prentis	C. B. Ticehurst
	St. J. A. M. Tolhurst	

April.

R. E. Brayne	W. R. Greening	B. B. Metcalfe
A. T. Densham	M. Leckie	E. L. R. Norton
M. M. Earle	F. B. Lowe	J. L. Rankine
N. Flower	J. H. Mayston	I. D. Stamp
	R. R. Walker	

July.

S. H. C. Air	W. C. M. Dickey	C. F. L. Leipoldt
H. P. Aubrey	J. G. Hodgson	E. P. Minett
R. G. Chase	E. P. H. Joynt	J. G. Phillips
H. B. Carlyll	H. F. Joynt	M. A. Rahman
L. Croft	P. P. Kolaporewalla	J. N. Watson

October.

W. W. Cook	A. N. Leeming	M. J. Rattray
G. W. Dryland	H. H. Moyle	S. McK. Saunders
H. J. Henderson	B. H. Palmer	G. G. Timpson
E. B. Hinde	M. D. Price	R. Willan

**Royal College of Surgeons of England.**

*Final Examination for the Fellowship.*

D. T. Barry		S. E. Denyer
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*Primary Examination for the Fellowship.*

H. L. Attwater	J. L. Johnston	L. C. Panting
W. Johnson	H. B. Kent	J. G. Saner
	T. D. M. Stout.	

*Final Examination for the Membership.*

January.

G. F. E. Allison	C. E. M. Jones	R. J. Reynolds
H. K. Digby	W. P. H. Munden	J. T. Smalley
H. G. Gibson	J. E. Prentis	C. B. Ticehurst
	St. J. A. M. Tolhurst	

April.

R. E. Brayne	W. R. Greening	B. B. Metcalfe
A. T. Densham	M. Leckie	E. L. R. Norton
M. M. Earle	F. B. Lowe	J. L. Rankine
N. Flower	J. H. Mayston	I. D. Stamp
	R. R. Walker	

July.

S. H. C. Air	W. C. M. Dickey	C. F. L. Leiboldt
H. P. Aubrey	J. G. Hodgson	E. P. Minett
R. G. Chase	E. P. H. Joynt	J. G. Phillips
H. B. Carlyll	H. F. Joynt	M. A. Rahman
L. Croft	P. P. Kolaporewalla	J. N. Watson

October.

W. W. Cook	A. N. Leeming	M. J. Rattray
G. W. Dryland	H. H. Moyle	S. McK. Saunders
H. J. Henderson	B. H. Palmer	G. G. Timpson
E. B. Hinde	M. D. Price	R. Willan

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EXAMINATIONS FOR THE L.D.S. ENGLAND.

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*Final Examination.*

May.

Parts I. and II.

E. L. Brown	A. H. Gabell	L. A. B. Moore
H. J. Dear	R. Hope	R. Redpath
	H. C. Visick	

Part I. only

R. J. Gibbings	C. R. M. Peaty	H. V. Sharp
A. F. Hochapfel	P. J. Proud	I. S. Spain
V. Masters	E. G. Robertson	H. Walker

Part II. only.

*E. P. Barnett	*H. T. Reeve	*T. L. Smith
*R. A. Glindon	*B. B. Samuel	

November.

Parts I. and II.

J. W. Doherty	H. J. Dumayne	I. Levy
W. A. Dredge	G. Hunt	

Part I. only.

W. F. Boxall	F. O. Hume	W. S. Rutter
S. W. Chetwood	C. C. Jones	H. P. Tait
F. N. Doubleday	W. Grant Oliver	W. F. Whiteley
A. M. Henry	J. R. Palmer	R. M. Wormald

Part II. only.

*R. J. Gibbings	*P. J. Proud	*R. A. Scott
*A. F. Hochapfel	*E. G. Robertson	*H. V. Sharp
*C. R. M. Peaty	*C. R. Rudolf	*I. S. Spain
	*H. Walker	

*First Professional Examination.*

May.

*Mechanical Dentistry and Dental Metallurgy.*

F. B. Bull	W. A. Hodgson	A. J. Reynolds
S. W. Charles	P. S. Humm	J. Roberts
A. Cohen	W. A. James	E. Smith
H. Daw	W. J. Kennealy	E. E. Solomon
W. H. Edmonds	W. S. Lacey	H. G. Spain
J. D. George	F. A. Lowe	D. B. Tasker
H. V. Gibbons	A. P. Marsh	W. E. A. Tibbalds
L. B. Griffin	R. C. Morgan	E. A. Tomes
P. S. Harrison	R. W. Morrell	A. MacDonald Watson
	W. E. Watson	

*Mechanical Dentistry only.*

*R. Hope		*D. Y. Hylton		*A. Samuel
		A. J. Schaefer		

*Dental Metallurgy only.*

N. D. Clarke		F. H. Edey		J. W. Hall
		H. S. Pugh		

November.

*Mechanical Dentistry and Dental Metallurgy.*

P. C. Charlton		G. H. Hickman		H. E. Shepherd
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*Mechanical Dentistry only.*

*N. D. Clarke		*H. S. Pugh		T. Townend
---------------	--	-------------	--	------------

*Dental Metallurgy only.*

\*A. J. Schaefer

\* Denotes completion of Examination.

*Preliminary Science Examination.*

March.

J. W. Hall		P. S. Humm		W. J. Kennealy
		A. MacDonald Watson.		

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**Society of Apothecaries, London.**

A. Shepperd.

---

**Conjoint Examining Board in England—Diploma in Public Health.**

B. H. Wedd.

---

**Royal Army Medical Corps.**

G. Carlisle

| H. G. Gibson

---

**Indian Medical Service.**

F. A. Barker

| A. T. Densham  
A. B. Zorab

| P. K. Tarapore

## MEDALLISTS AND PRIZEMEN.

JULY, 1908.

*Open Scholarships in Arts.*

Cedric Sydney Lane Roberts, Cheltenham College, £100.

George Dunluce Eccles, Plymouth Technical School, £50.

*Open Scholarships in Science.*

John Finlayson Mackenzie, Preliminary Science Class, Guy's Hospital, £150.

Richard Douglas Passey, Preliminary Science Class, Guy's Hospital, £60.

Thomas Izod Bennett, Preliminary Science Class, Guy's Hospital, Certificate.

George Edward Genge-Andrews, Preliminary Science Class, Guy's Hospital, Certificate.

Skene Keith, Preliminary Science Class, Guy's Hospital, Certificate.

*Scholarship for University Students.*

John Godfrey Saner, B.A., Caius College, Cambridge, £50.

*Open Scholarships in Dental Mechanics.*

October, 1907, Charles Holme Barnett, £20.

May, 1908, Harold Harrison, £20.

*Junior Proficiency Prizes.*

Frank Cook, £20.

Edward Gustave Schlesinger, £15.

Abdel Hamid Gool, £10.

Herbert Leslie Hopkins, Certificate.

*The Beaney Prize for Pathology (1907).*

Kenelm Hutchinson Digby, £34.

Thomas Edmund Ashdown Carr, Certificate.

*The Michael Harris Prize for Anatomy.*

Edward Gustave Schlesinger, £10.

Abdel Hamid Gool, Certificate.

*The Wooldridge Memorial Prize for Physiology.*

Frank Cook, £10.

*Dental Prizes.*

*First Year's Students.*

James Alfred Wyllys Stuart, £10.

*Practical Dentistry Prize.*

William Archer Hodgson, £10.

Hubert Ernest Shepherd, Certificate.

*Golding-Bird Gold Medal and Scholarship in Bacteriology.*

Hugh Stolt, £20.

Herbert Cubitt Lucey, Certificate.

*Treasurer's Gold Medal for Clinical Medicine.*

Edward Leslie Martyn Lobb.

*Treasurer's Gold Medal for Clinical Surgery.*

Arthur Norman Leeming, Medal.

Gilbert Francis Syms, Certificate.

# THE PHYSICAL SOCIETY.

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**Honorary Vice-Presidents.**—J. F. Goodhart, M.D., LL.D., Sir H. G. Howse, M.S., P. H. Pye-Smith, M.D., F.R.S., G. H. Savage, M.D.

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**Hon. Secretaries.**—W. M. Mollison, M.C., G. W. Nicholson, M.D.

Session 1907-1908.—The Society's prize of £10 for the best essay read during the Session was divided: to Mr. J. Lee Atkinson, £5; Mr. G. H. K. Macalister and Mr. W. H. Trethowan received £2 10s. each.

The Treasurer's prize of £5 was awarded to Mr. R. G. Chase for his essay on the Diagnosis of Acute Abdominal Conditions.

The prize of £5 for the best specimens exhibited during the Session was divided: to Mr. G. W. Goodhart, £4, to Mr. C. A. Wood, £1.

## CLINICAL APPOINTMENTS HELD DURING THE YEAR 1907.

### HOUSE PHYSICIANS.

W. P. Purdom  
A. S. M. Palmer  
C. B. Ticehurst

R. Davies Colley  
W. H. Trethowan  
B. K. Nutman

H. F. Vandermin  
P. F. McEvedy

### HOUSE SURGEONS.

A. Alcock  
W. Welchman  
G. F. Stebbing

T. B. Layton  
E. Wragg  
K. H. Digby

A. S. B. Bankart  
S. W. Daw  
J. S. Cooper

### ASSISTANT HOUSE SURGEONS.

E. Morgan  
W. H. Miller  
G. F. Stebbing  
P. P. Laidlaw  
C. E. M. Jones

R. P. Rowlands  
S. W. Daw  
J. S. Bookless  
N. Flower  
R. Evans  
C. F. L. Leipoldt

W. H. S. Burney  
W. P. Munden  
J. T. Smalley  
C. H. Rippmann  
M. M. Earle

### OUT-PATIENTS' OFFICERS.

A. S. B. Bankart  
W. Welchman  
W. H. Trethowan  
B. K. Nutman

A. S. M. Palmer  
P. F. McEvedy  
E. Wragg  
G. F. Stebbing

H. F. Vandermin  
R. P. Rowlands  
K. H. Digby  
A. Zorab

OBSTETRIC RESIDENTS.

P. S. Mills	H. C. Malleson	C. A. L. Mayer
E. M. Harrison	L. G. Davies	E. B. Smith
A. Alcock	G. H. K. Macalister	

CLINICAL ASSISTANTS.

J. S. Bookless	S. W. Daw	P. F. McEvedy
G. F. Stebbing	W. H. Trethowan	E. Wragg
K. H. Digby	P. P. Laidlaw	B. K. Nutman
C. H. Rippmann	J. T. Smalley	A. Zorab
M. M. Earle	G. W. Goodhart	C. E. M. Jones
C. F. L. Leipoldt	C. B. Ticehurst	R. R. Walker
R. G. Chase	N. Flower	M. Leckie
W. P. Munden	H. J. Smith	J. N. Watson

CLINICAL ASSISTANTS IN THE MEDICAL WARDS.

J. L. Rankine	C. F. L. Leipoldt	H. J. Henderson
St. J. A. M. Tolhurst	W. W. Cook	G. W. Dryland
B. H. Palmer	A. N. Leeming	T. E. A. Carr
J. W. Grice	W. G. Pinching	H. A. Sanford
M. E. Ball	R. P. M. Roberts	H. Stott

CLINICAL ASSISTANTS IN THE SURGICAL WARDS.

J. W. Grice	C. W. Greene	E. P. Minett
H. F. Joynt	J. H. Ryffel	P. H. Fuller
F. J. Wheeler	R. B. Dawson	C. S. E. Wright
T. N. Wood	H. H. Moyle	H. Franklin
S. K. Poole	J. K. Helm	

CLINICAL ASSISTANTS IN THE MEDICAL OUT-PATIENTS.

J. T. Smalley	D. Isaacs	C. W. R. Preston
L. L. C. Reynolds		

SURGEONS' DRESSERS.

T. Evans	R. A. Rankine	G. F. Syms
H. E. Lucey	J. F. Young	R. P. M. Roberts
J. Walker	E. R. Stone	H. B. Carter
H. J. Cutler	A. N. Leeming	M. E. Ball
J. B. Dunning	C. H. Mills	E. P. L. Hughes
L. T. Dean	P. G. V. Pedrick	E. M. Lobb
C. S. E. Wright	F. J. Wheeler	F. J. Cutler
A. E. Lees	J. F. Kolaporewalla	K. H. Hole
H. Chapple	H. E. H. Mitchell	H. O. Brookhouse
P. S. Price	D. Allan	S. S. Brook
L. Mandel	H. Shahin	H. R. Mullins
H. A. Sanford	V. F. Hutchinson	W. Johnson
D. C. Druitt	H. W. Heasman	A. E. Rayner
H. J. Janmahomed	H. Lee	A. D. Vernon Taylor
T. Stansfield	S. H. Browning	W. E. Wallis
V. Townrow	S. J. Darke	T. F. Brown
C. C. Holman	F. R. L. Atkins	A. E. P. Cheesman
D. Reynolds	C. M. Plumptre	L. W. Evans
F. C. V. Thompson	A. L. George	R. G. Oram
S. H. Browning	C. G. Sprague	M. M. Adams
M. M. Cowasjee	A. H. Khalakdina	H. B. Kent
A. D. Williams	A. H. Crook	H. R. Bastard



OPHTHALMIC DRESSERS.

T. N. Wood	H. B. Carlyll	M. D. Price
E. B. Hinde	S. K. Poole	M. K. Nelson
E. P. Minett	J. A. C. Greene	J. L. D. Hughes
C. E. Price	J. B. Martin	B. H. Palmer
E. W. Ewing	A. L. Foster	H. Shahin
G. W. Dryland	E. Abdy Collins	H. C. Lucey
L. T. Baker	F. Morres	R. Edsall
H. E. Perkins	H. A. Sanford	C. A. Basker
C. S. E. Wright		

DRESSERS IN THE THROAT DEPARTMENT.

M. M. Earle	A. T. Densham	R. R. Walker
E. B. Hinde	C. H. Rippmann	J. N. Watson
W. H. Miller	A. F. W. Denning	G. F. E. Allison
H. J. Smith	N. Flower	B. Muir
C. A. Basker	H. J. Henderson	S. McK. Saunders
E. P. H. Joynt	H. F. Joynt	R. G. Chase
H. Stott	W. W. Cook	J. B. Martin
H. B. Carlyll	M. R. Dobson	L. T. Dean

MEDICAL WARD CLERKS.

A. A. Greenwood	J. R. Perdrau	J. L. Atkinson
W. T. Clarke	G. F. Haycraft	V. T. P. Webster
F. Kahlenberg	L. Bromley	H. L. Duke
H. F. Percival	W. S. Kidd	H. Platts
W. L. Hibbert	D. A. Mitchell	C. Weller
C. H. Catto	F. C. Endean	C. C. Tudge
W. Ledlie	H. L. Attwater	F. D. Saner
W. E. Williams	F. J. Killard-Leavey	Q. H. Richardson
H. R. Bastard	R. G. Oram	M. M. Adams
F. C. V. Thompson	F. R. L. Atkins	M. M. Cowasjee
S. J. Darke	R. A. Rankine	C. A. Wood
A. E. P. Cheesman	T. F. Brown	H. B. Kent
C. G. Sprague	A. R. Khalakdina	A. L. George
A. H. Crook	L. W. Evans	C. C. Holman
C. M. Plumptre	A. D. Williams	N. A. D. Sharp
C. H. Crump	E. L. Elliott	A. L. Fitzmaurice
C. Witts	H. Steinbach	A. G. H. Burton
P. C. Field	J. L. Johnston	G. H. Peall
A. D. Vernon Taylor	T. Stansfield	S. H. Browning
H. W. Heasman	H. I. Janmahomed	V. Townrow
D. C. Druitt	W. E. Wallis	A. E. Rayner
W. H. Watson	H. Lee	C. F. Searle
H. F. Haycraft	H. O. Brookhouse	H. E. H. Mitchell
D. Reynolds	A. E. Lees	P. S. Price
R. C. H. Francis		

SURGICAL WARD CLERKS.

J. R. Perdrau	J. L. Atkinson	G. F. Haycraft
V. T. P. Webster	L. Bromley	H. L. Duke
H. F. Percival	W. T. Clarke	F. Kahlenberg
W. H. Watson	C. H. Crump	E. L. Elliott
A. L. Fitzmaurice	J. L. Johnston	G. H. Peall
A. G. H. Burton	J. C. D. Sharp	T. J. Killard-Leavey
H. Steinbach	P. C. Field	W. S. Kidd
W. L. Hibbert	D. A. Mitchell	C. Weller
W. H. Catto	C. C. Tudge	W. E. Williams
W. Reynolds	H. L. Attwater	F. D. Saner
W. Ledlie	F. E. Endean	H. Platts
R. P. Ballard	M. A. E. Duvivier	G. Macted
A. N. Cox	H. Gardiner	A. L. Saul
G. H. Hunt	J. H. Owen	N. L. M. Reader
P. E. Patey	F. S. D. Berry	

ASSISTANT SURGEONS' DRESSERS.

V. Townrow	J. L. Johnston	C. H. Crump
T. Stansfield	H. Lee	S. H. Browning
H. I. Janmahomed	A. D. V. Taylor	A. E. Rayner
A. R. Khalakdina	W. E. Wallis	C. F. Searle
R. G. Oram	H. W. Heasman	D. C. Druitt
A. E. R. Cheesman	F. R. L. Atkins	Q. H. Richardson
C. G. Sprague	C. C. Holman	L. W. Evans
A. D. Williams	R. C. H. Francis	R. A. Rankine
H. B. Kent	M. M. Adams	H. R. Bastard
A. L. George	T. F. Brown	A. H. Crook
S. J. Darke	F. C. V. Thompson	C. M. Plumptre
C. A. Wood	S. L. Randolph	M. M. Cowasjee
W. T. Clarke	F. Kahlenberg	G. F. Haycraft
L. Bromley	H. L. Duke	J. R. Perdrau
V. T. P. Webster	J. L. Atkinson	H. F. Percival
A. A. Greenwood	E. L. Elliott	A. G. Burton
A. L. Fitzmaurice	P. C. Field	W. H. Watson
G. H. Peall	N. D. Sharp	H. Steinbach

ASSISTANT SURGEONS' CLERKS.

H. L. Attwater	W. Ledlie	F. C. V. Thompson
W. Reynolds	J. L. Atkinson	J. C. D. Sharp
J. L. Johnston	J. W. Williams	G. R. Hind
T. D. M. Stout	G. Dunderdale	

DENTAL SURGEONS' DRESSERS.

H. F. Joynt	E. L. R. Norton	E. B. Hinde
B. Wallis	S. K. Poole	A. N. Leeming
E. P. Joynt	G. F. Syms	M. A. Rahman
H. R. Mullins	W. Johnson	A. F. W. Denning

CLERKS IN THE SKIN DEPARTMENT.

H. A. Shahin	A. Zorab	T. F. Brown
F. R. L. Atkins	L. Bromley	F. Kahlenberg

**AURAL SURGEONS' DRESSERS**

C. H. Rippmann	A. T. Densham	F. W. Hogarth
B. Wallis	J. H. Mayston	P. H. Joynt
C. A. Barker	H. F. Joynt	R. G. Chase
H. B. Carlyll	M. Leckie	C. E. Price
	M. A. Rahman	

**POST MORTEM CLERKS.**

A. W. F. Denning	L. L. C. Reynolds	F. H. Fuller
W. Johnson	J. H. Ryffel	J. B. Martin
S. H. C. Air	M. J. Rattray	H. E. Perkins
R. C. Edsall	H. C. Lucey	J. B. Dunning
B. H. Palmer	H. B. Carter	H. Stott
F. W. Hogarth	A. H. Crook	E. L. M. Lobb
E. R. Stone	C. A. Wood	H. O. Brookhouse
K. H. Hole	R. P. M. Roberts	P. S. Price
H. Chapple	H. A. Sanford	H. E. H. Mitchell
	F. J. Wheeler	

**OBSTETRIC DRESSERS.**

H. J. Henderson	K. H. Digby	N. Flower
G. W. Dryland	J. T. Smalley	C. H. Marshall
W. W. Cook	E. Abdy Collins	H. Stott
C. E. Price	J. N. Watson	E. L. M. Lobb
L. Croft	M. J. Rattray	E. R. Stone
H. E. Perkins	L. T. Baker	M. R. Dobson
S. H. C. Air	J. F. Young	F. J. Cutler
H. B. Carter	A. N. Leeming	J. B. Dunning
T. Evans	S. S. Brook	A. E. Lees
W. Johnson	L. Mandel	H. I. Janmahomed

**CLERKS TO ANÆSTHETISTS.**

E. P. L. Hughes	H. C. Lucey	E. R. Stone
R. B. Dawson	F. J. Wheeler	A. W. Ewing
G. F. Syms	E. B. Hinde	C. H. Marshall
C. G. Pinching	F. W. Hogarth	M. R. Dobson
H. G. Gibson	P. J. Kolaporewalla	W. Johnson
B. Muir	A. F. Denning	C. G. Douglas
J. B. Martin	F. B. Lowe	A. H. V. St. John
A. E. Lees	J. B. Ball	H. F. Joynt
H. E. H. Mitchell	J. F. Young	M. Leckie
F. H. Fuller	M. Earle	A. C. Dickson
T. Evans	C. E. Price	C. W. Greene
H. E. Perkins	R. C. V. Edsall	J. B. Dunning
T. H. Edey	H. A. Sanford	C. S. E. Wright
F. J. Cutler	H. B. Carlyll	P. S. Price
W. H. Watson	W. E. Wallis	H. Shahin
H. Stott	F. C. V. Thompson	V. P. Hutchinson
J. Walker	F. R. L. Atkins	M. E. Ball
D. Reynolds	A. D. V. Taylor	A. R. Khalakdina
C. A. Wood	S. McK. Saunders	S. H. Browning
R. A. Rankine	H. O. Brookhouse	L. T. Dean
P. V. G. Pedrick	H. W. Heasman	J. F. Young
L. Mandel	H. Lee	R. Franklin
H. R. Mullins	E. L. M. Lobb	W. W. Cook
H. I. Janmahomed		

**OPHTHALMIC HOUSE SURGEONS.**

R. Edridge	P. S. Mills	C. A. L. Mayer
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# DENTAL SCHOOL

## CLINICAL APPOINTMENTS HELD DURING THE YEAR 1907.

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### HOUSE SURGEONS.

H. J. Dear    |    J. R. D. Ditch    |    I. Margolies    |    H. O. Visick

### ASSISTANT HOUSE SURGEONS.

H. J. Dear	R. J. Gibbings	W. Grant Oliver
J. W. Doherty	G. Hunt	I. S. Spain
F. N. Doubleday	R. M. Hunt	

### DEMONSTRATORS IN THE CONSERVATION ROOM.

F. N. Doubleday	L. A. B. King	E. Smith
H. V. Gibbons	R. M. King	E. E. Solomon
W. E. Guilding	I. Levy	H. P. Tait
G. Hunt	J. Roberts	D. B. Tasker

### ASSISTANT DEMONSTRATORS IN DENTAL MECHANICS.

R. J. Gibbings    |    A. F. Hochapfel    |    R. M. Wormald

### ASSISTANT DEMONSTRATORS IN DENTAL METALLURGY.

J. W. Doherty    |    I. S. Spain    |    H. Walker

### ASSISTANT DEMONSTRATORS IN DENTAL MICROSCOPY.

F. N. Doubleday    |    R. J. Gibbings    |    H. Walker

### DRESSERS IN THE GAS ROOM.

E. Barnett	W. A. Hodgson	J. Roberts
W. F. Boxall	F. O. Hume	E. G. Robertson
S. W. Charles	G. Hunt	A. H. Rothenberg
N. D. Clarke	D. Y. Hylton	A. Samuel
A. Cohen	W. A. James	A. L. Saul
J. W. Doherty	C. C. Jones	H. E. Shepherd
F. N. Doubleday	W. J. Kennealy	E. Smith
W. A. Dredge	L. A. B. King	E. E. Solomon
F. H. Edey	R. M. King	H. Sturton
P. R. Eskell	W. S. Lacey	E. W. Sumpter
A. H. Gabell	I. Levy	H. P. Tait
R. J. Gibbings	V. Masters	D. B. Tasker
H. V. Gibbons	R. C. Morgan	W. E. A. Tibbalds
L. B. Griffin	R. W. Morrell	E. A. Tomes
W. E. Guilding	J. R. Palmer	T. Townsend
P. Harrison	C. R. M. Peaty	H. Walker
P. R. Helyar	P. J. Proud	W. E. Watson
A. M. Henry	H. S. Pugh	W. F. Whiteley
A. F. Hochapfel	A. J. Reynolds	

# DRESSERS IN THE EXTRACTION ROOM.

C. H. Bradnam	J. W. Hall	G. H. Rowley
F. B. Bull	P. S. Harrison	C. F. L. Ruck
S. W. Charles	A. M. Henry	A. J. Schaefer
N. D. Clarke	W. A. Hodgson	H. E. Shepherd
A. Cohen	P. S. Humm	E. E. Solomon
H. Daw	A. P. L. Johnson	H. G. Spain
G. V. Dymott	W. S. Lacey	J. A. W. Stuart
F. H. Edey	F. A. Lowe	E. W. Sumpter
N. Edgar	A. P. Marsh	W. A. Thompson
W. H. Edmunds	R. C. Morgan	H. Thornton
T. L. Fiddick	R. W. Morrell	W. E. A. Tibbalds
F. L. Furse	H. S. Morris	E. A. Tomes
J. D. George	G. H. H. Phillips	C. C. A. Wale
H. V. Gibbons	H. S. Pugh	N. S. H. Warner
H. H. Glover	A. J. Reynolds	A. M. Watson
L. B. Griffin	J. Roberts	

# CASUALTY DRESSERS.

F. B. Bull	W. A. James	A. L. Saul
S. W. Charles	L. J. Kemp	A. J. Schaefer
N. D. Clarke	W. J. Kennealy	H. E. Shepherd
A. Cohen	W. S. Lacey	E. Smith
F. H. Edey	F. A. Lowe	E. E. Solomon
J. D. George	A. P. Marsh	H. G. Spain
H. V. Gibbons	R. C. Morgan	E. W. Sumpter
L. B. Griffin	R. W. Morrell	W. E. A. Tibbalds
J. W. Hall	H. S. Pugh	E. A. Tomes
P. Harrison	A. J. Reynolds	T. Townend
G. H. Hickman	J. Roberts	W. E. Watson
W. A. Hodgson	G. H. Rowley	

# DRESSERS IN THE CONSERVATION ROOM.

E. J. Archer	W. A. Hodgson	R. Redpath
E. Barnett	F. O. Hume	H. T. Reeve
W. F. Boxall	P. S. Humm	A. J. Reynolds
F. B. Bull	G. Hunt	J. Roberts
S. W. Charles	D. Y. Hylton	E. G. Robertson
S. W. Chetwood	O. G. Iliffe	N. P. Rodgers
N. D. Clarke	W. A. James	G. H. Rowley
A. Cohen	C. C. Jones	C. Rudolf
J. W. Doherty	L. J. Kemp	A. Samuel
F. N. Doubleday	W. J. Kennealy	B. B. Samuel
W. A. Dredge	L. A. B. King	A. L. Saul
F. H. Edey	R. M. King	A. J. Schaefer
P. R. Eskell	W. S. Lacey	E. E. Solomon
A. H. Gabell	I. Levy	E. Smith
J. D. George	F. A. Lowe	I. S. Spain
R. J. Gibbings	M. J. Marks	H. Sturton
H. V. Gibbons	A. P. Marsh	E. W. Sumpter
R. A. Glindon	V. Masters	H. P. Tait
L. B. Griffin	L. B. Moore	D. B. Tasker
W. E. Guilding	R. C. Morgan	H. C. Visick
P. S. Harrison	R. W. Morrell	H. Walker
P. R. Helyar	J. R. Palmer	W. E. Watson
A. M. Henry	P. J. Proud	W. F. Whiteley
G. H. Hickman	H. S. Pugh	R. M. Wormald
A. F. Hochapfel		

PROBATIONARY DRESSERS.

S. W. Charles  
N. D. Clarke  
W. H. Edmunds  
J. D. George  
L. B. Griffin  
J. W. Hall  
W. A. Hodgson

W. S. Lacey  
F. A. Lowe  
F. E. Lowe  
A. P. Marsh  
P. S. Pugh  
A. J. Reynolds  
J. Roberts

G. H. Rowley  
A. J. Schaefer  
H. S. Spain  
W. E. A. Tibbalds  
E. A. Tomes  
A. McD. Watson  
W. E. Watson

# GUY'S HOSPITAL.

## MEDICAL AND SURGICAL STAFF.

1908.

**Consulting Physicians.**—SIR SAMUEL WILKS, BART., M.D., LL.D., F.R.S.; F. W. PAVY, M.D., LL.D., F.R.S.; P. H. PYE-SMITH, M.D., F.R.S.; J. F. GOODHART, M.D., LL.D.; F. TAYLOR, M.D.

**Consulting Surgeons.**—THOMAS BRYANT, M.Ch.; SIR H. G. HOWSE, M.S.; W. H. A. JACOBSON, M.Ch.; R. CLEMENT LUCAS, B.S.; C. H. GOLDING-BIRD, M.B.

**Consulting Obstetric Physician.**—A. L. GALABIN, M.D.

**Consulting Physician for Mental Diseases.**—G. H. SAVAGE, M.D.

**Consulting Ophthalmic Surgeons.**—C. HIGGINS, Esq.; W. A. BRAILEY, M.D.

**Consulting Aural Surgeon.**—W. LAIDLAW PURVES, M.D.

**Consulting Dental Surgeon.**—F. NEWLAND-PEDLEY, Esq.

**Consulting Anæsthetist.**—TOM BIRD, Esq.

**Physicians & Assistant Physicians.**

W. HALE WHITE, M.D.

G. NEWTON PITT, M.D.

SIR E. COOPER PERRY, M.D.

L. E. SHAW, M.D.

J. FAWCETT, M.D.

A. P. BEDDARD, M.D.

H. S. FRENCH, M.D.

A. F. HERTZ, M.D.

**Obstetric Physicians.**

P. HORROCKS, M.D.

J. H. TARGETT, M.S.

**Assistant Obstetric Physician.**

G. BELLINGHAM SMITH, M.B., B.S.

**Physician for Mental Diseases.**

MAURICE CRAIG, M.D.

**Physician in Charge of Skin Department.**

SIR E. COOPER PERRY, M.D.

**Anæsthetists.**

G. ROWELL, Esq.

H. F. LANCASTER, M.D.

C. J. OGLE, Esq.

H. M. PAGE, Esq.

F. E. SHIPWAY, M.D.

W. M. MOLLISON, M.C.

A. R. THOMPSON, M.B., Ch.M.

R. DAVIES-COLLEY, M.B., B.C.

P. P. LAIDLAW, B.C.

E. C. HUGHES, M.C.

**Bacteriologist.**

J. W. H. EYRE, M.D.

**Medical Registrars and Tutors.**

H. C. CAMERON, M.D.

C. H. RIPPMMANN, B.C.

**Obstetric Registrar and Tutor.**

R. DAVIES-COLLEY, M.B., B.C.

**Resident Surgical Officer.**

S. W. DAW, Esq.

**Curator of the Museum.**

J. FAWCETT, M.D.

**Warden of the College.**

W. M. MOLLISON, M.C.

**Surgeons & Assistant Surgeons.**

CHARTERS J. SYMONDS, M.S.

W. ARBUTHNOT LANE, M.S.

L. A. DUNN, M.S.

SIR ALFRED FRIPP, M.S., C.B., K.C.V.O.

F. J. STEWARD, M.S.

C. H. FAGGE, M.S.

R. P. ROWLANDS, M.S.

P. TURNER, M.S.

**Ophthalmic Surgeons.**

H. L. EASON, M.S., M.D.

A. W. ORMOND, Esq.

**Surgeon in Charge of Throat Department.**

F. J. STEWARD, M.S.

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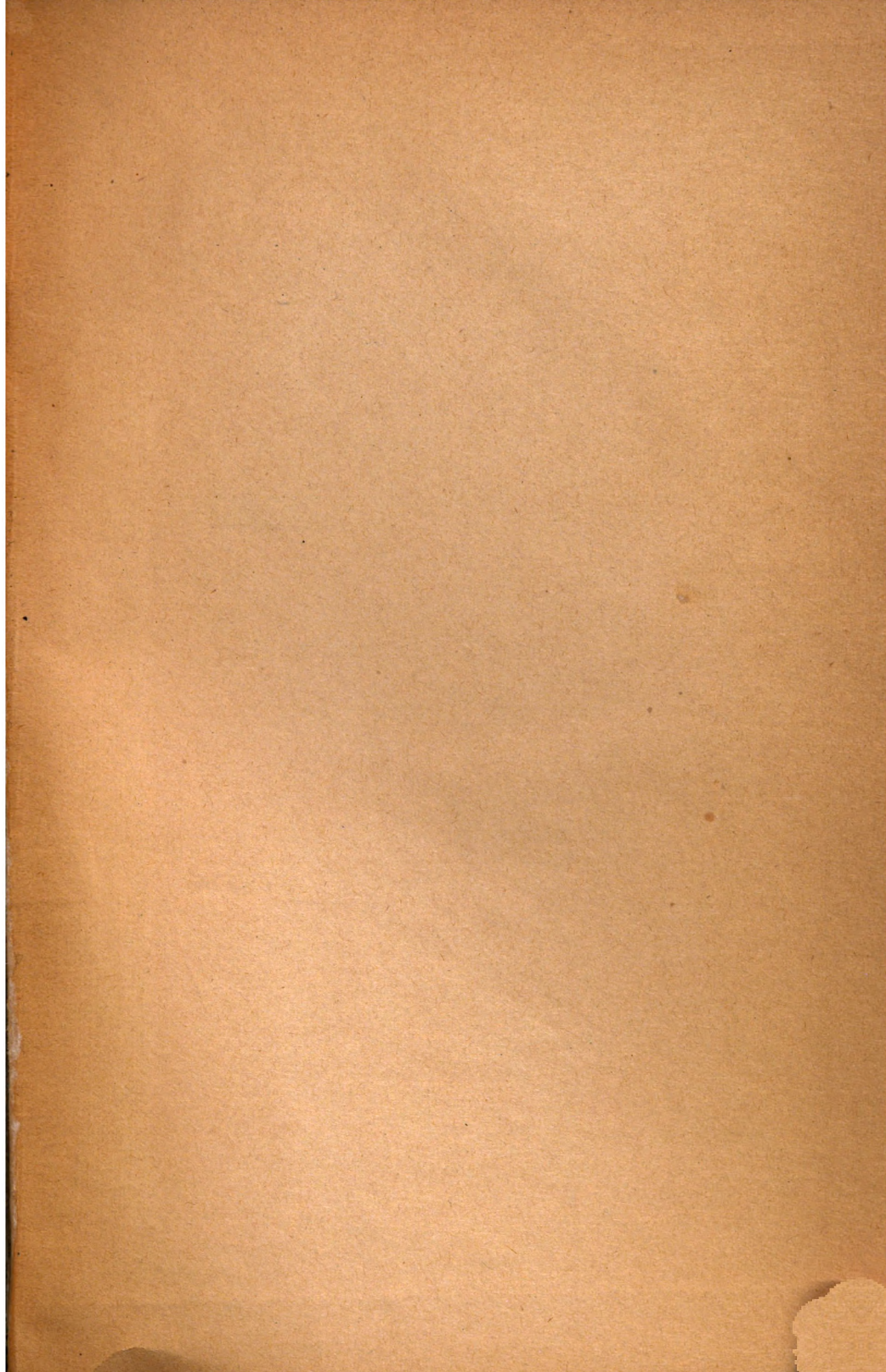
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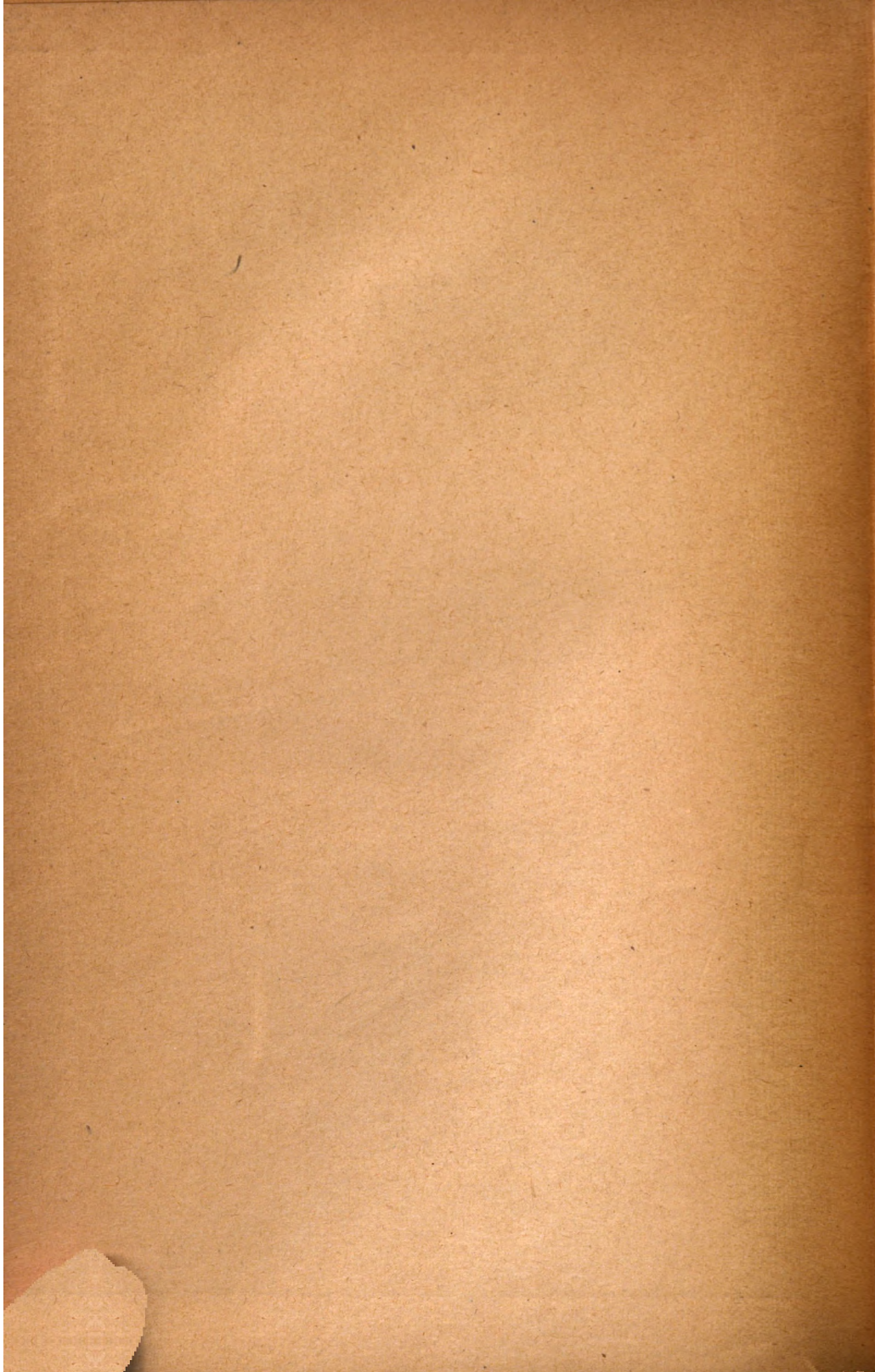
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